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* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS	1		Web Page for STN Seminar Schedule - N. America
NEWS	2	JAN 02	STN pricing information for 2008 now available
NEWS	3	JAN 16	CAS patent coverage enhanced to include exemplified prophetic substances
NEWS	4	JAN 28	USPATFULL, USPAT2, and USPATOLD enhanced with new custom IPC display formats
NEWS	5	JAN 28	MARPAT searching enhanced
NEWS	6	JAN 28	USGENE now provides USPTO sequence data within 3 days of publication
NEWS	7	JAN 28	TOXCENTER enhanced with reloaded MEDLINE segment
NEWS	8	JAN 28	MEDLINE and LMEDLINE reloaded with enhancements
NEWS	9	FEB 08	STN Express, Version 8.3, now available
NEWS	10	FEB 20	PCI now available as a replacement to DPCI
NEWS	11	FEB 25	IFIREF reloaded with enhancements
NEWS	12	FEB 25	IMSPRODUCT reloaded with enhancements
NEWS	13	FEB 29	WPINDEX/WPIDS/WPIX enhanced with ECLA and current U.S. National Patent Classification
NEWS	14	MAR 31	IFICDB, IFIPAT, and IFIUDB enhanced with new custom IPC display formats
NEWS	15	MAR 31	CAS REGISTRY enhanced with additional experimental spectra
NEWS	16	MAR 31	CA/CAplus and CASREACT patent number format for U.S. applications updated
NEWS	17	MAR 31	LPCI now available as a replacement to LDPCI
NEWS	18	MAR 31	EMBASE, EMBAL, and LEMBASE reloaded with enhancements
NEWS	19	APR 04	STN AnaVist, Version 1, to be discontinued
NEWS	20	APR 15	WPIDS, WPINDEX, and WPIX enhanced with new predefined hit display formats
NEWS	21	APR 28	EMBASE Controlled Term thesaurus enhanced
NEWS	22	APR 28	IMSRESEARCH reloaded with enhancements

NEWS EXPRESS FEBRUARY 08 CURRENT WINDOWS VERSION IS V8.3,
AND CURRENT DISCOVER FILE IS DATED 20 FEBRUARY 2008

NEWS HOURS	STN Operating Hours Plus Help Desk Availability
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NEWS IPC8	For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that specific topic.

* * * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 13:04:25 ON 13 MAY 2008

=> file casreact
FILE 'CASREACT' ENTERED AT 13:05:03 ON 13 MAY 2008
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FILE CONTENT:1840 - 10 May 2008 VOL 148 ISS 20

New CAS Information Use Policies, enter HELP USAGETERMS for details.

****
*
*   CASREACT now has more than 13.8 million reactions   *
*
****

Some CASREACT records are derived from the ZIC/VINITI database (1974-1999)
provided by InfoChem, INPI data prior to 1986, and Biotransformations
database compiled under the direction of Professor Dr. Klaus Kieslich.

This file contains CAS Registry Numbers for easy and accurate substance
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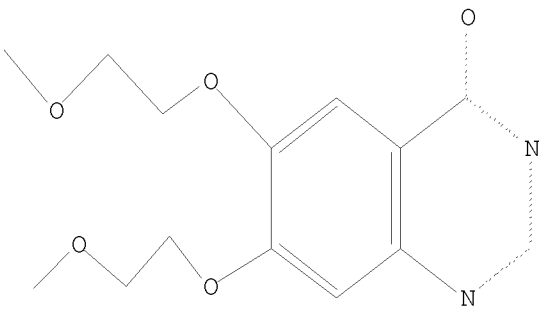
=>
Uploading C:\Program Files\Stnexp\Queries\10565981.str

L1   STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1   STR



Structure attributes must be viewed using STN Express query preparation.

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SAMPLE SEARCH INITIATED 13:05:38 FILE 'CASREACT'
SCREENING COMPLETE -   0 REACTIONS TO VERIFY FROM   0 DOCUMENTS

100.0% DONE   0 VERIFIED   0 HIT RXNS   0 DOCS

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SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED VERIFICATIONS:         0 TO        0
PROJECTED ANSWERS:               0 TO        0

L2            0 SEA SSS SAM L1 (     0 REACTIONS)

=> s l1 full
FULL SEARCH INITIATED 13:06:07 FILE 'CASREACT'
SCREENING COMPLETE -      247 REACTIONS TO VERIFY FROM       33 DOCUMENTS

100.0% DONE     247 VERIFIED      80 HIT RXNS                      10 DOCS
SEARCH TIME: 00.00.01

L3           10 SEA SSS FUL L1 (    80 REACTIONS)

=> d help

The following are valid formats:

ABS -------- GI and AB
ALL -------- BIB, AB, IND, RE, Single-step Reactions
APPS ------- AI, PRAI
BIB -------- AN, plus Bibliographic Data
CAN -------- List of CA abstract numbers without answer numbers
CBIB ------- AN, plus Compressed Bibliographic Data
DALL ------- ALL, delimited (end of each field identified)
IABS ------- ABS, indented with text labels
IALL ------- ALL, indented with text labels
IBIB ------- BIB, indented with text labels
IND -------- Indexing data
IPC -------- International Patent Classifications
ISTD ------- STD, indented with text labels
OBIB -------- AN, plus Bibliographic Data (original)
OIBIB ------- OBIB, indented with text labels

SBIB -------- BIB, no citations
SIBIB ------- IBIB, no citations

MAX -------- Same as ALL
PATS ------- PI, SO
SCAN ------- TI and FCRD (random display, no answer number.  SCAN
             must be entered on the same line as DISPLAY, e.g.,
             D SCAN.)
SSRX ------- Single-Step Reactions (Map, Diagram, and Summary for
             all single-step reactions)
STD -------- BIB, IPC, and NCL

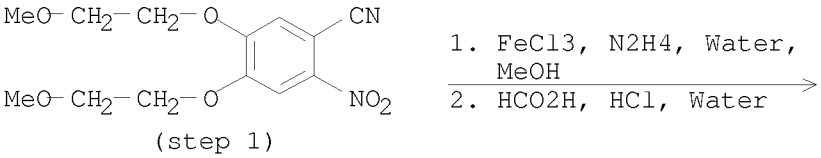
CRD -------- Compact Display of All Hit Reactions
CRDREF ----- Compact Reaction Display and SO, PY for Reference
FHIT ------- Reaction Map, Diagram, and Summary for first
             hit reaction
FHITCBIB --- FHIT, AN plus CBIB
FCRD ------- First hit in Compact Reaction Display (CRD) format
FCRDREF ---- First hit in Compact Reaction Display (CRD) format with
             CA reference information (SO, PY).  (Default)
FPATH ------ PATH, plus Reaction Summary for the "long path"
FSPATH ----- SPATH, plus Reaction Summary for the "short path"
HIT -------- Reaction Map, Reaction Diagram, and Reaction
             Summary for all hit reactions and fields containing
```

hit terms
OCC -------- All hit fields and the number of occurrences of the hit terms in each field. Includes total number of HIT, PATH, SPATH reactions. Labels reactions that have incomplete verifications.
PATH ------- Reaction Map and Reaction Diagram for the "long path". Displays all hit reactions, except those whose steps are totally included within another hit reaction which is displayed
RX --------- Hit Reactions (Map, Diagram, Summary for all hit reactions)
RXG -------- Hit Reaction Graphics (Map and Diagram for all hit reactions)
RXL -------- Hit Reaction Long (Map, Diagram, Summary for all hit reactions)
RXS -------- Hit Reaction Summariers (Map and Summary for all hit reactions)
SPATH ------ Reaction Map and Reaction Diagram for the "short path". Displays all single step reactions which contain a hit substance. Also displays those multistep reactions that have a hit substance in both the first and last steps of the reaction, except for those hit reactions whose steps are totally included within another hit reaction which is displayed

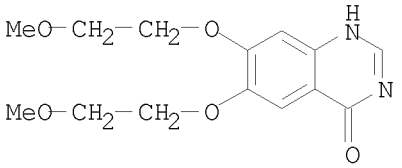
To display a particular field or fields, enter the display field codes. For a list of the display field codes, enter HELP DFIELDS at an arrow prompt (=>). Examples of combinations include: D TI; D BIB RX; D TI, AU, FCRD. The information is displayed in the same order as the specification. All of the formats, except CRD, CRDREF, FHIT, PATH, FPATH, SPATH, FSPATH, FCRD, FCRDREF, HIT, RX, RXG, RXS, SCAN, and OCC, may be used with the DISPLAY command to display the record for a specified Accession Number.

L3 ANSWER 1 OF 10 CASREACT COPYRIGHT 2008 ACS on STN

RX(14) OF 57



(step 1)



81%

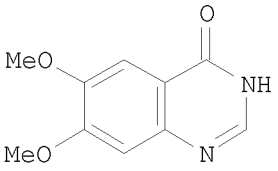
REF: Heterocycles, 71(1), 39-48; 2007
NOTE: key intermediate
CON: STAGE(1) 1 hour, reflux; 2 hours, reflux
STAGE(2) room temperature -> 130 deg C; 3 hours, 130 deg C

=> d cbib abs crd 1-10

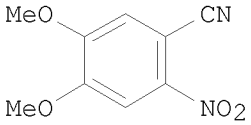
L3 ANSWER 1 OF 10 CASREACT COPYRIGHT 2008 ACS on STN

146:421938 One-pot conversion of 2-nitrobenzonitriles to quinazolin-4(3H)-ones and synthesis of gefitinib and erlotinib hydrochloride. Chandregowda, Venkateshappa; Rao, Gudapati Venkateswara; Reddy, Goukanapalli Chandrasekara (Vittal Mallya Scientific Research Foundation, Bangalore, 560004, India). Heterocycles, 71(1), 39-48 (English) 2007. CODEN: HTCYAM. ISSN: 0385-5414. Publisher: Japan Institute of Heterocyclic Chemistry.

GI



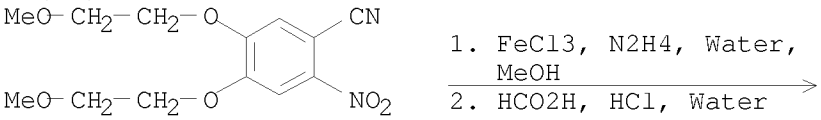
I



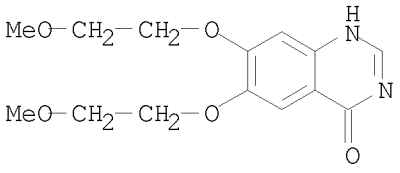
II

AB A simple and efficient one-pot conversion of 2-nitrobenzonitriles to quinazolin-4(3H)-ones involving reduction, formylation, hydrolysis and cyclization is reported. E.g., quinazolin-4(3H)-one derivative I was prepared with 85% yield by reacting the corresponding 2-nitrobenzonitrile II with hydrazine using FeCl3 in MeOH/H2O followed by treating the reaction mixture with formic acid and HCl. These quinazolinones have been used for making in economical way the anticancer drug mols. gefitinib (Iressa) and erlotinib HCl (Tarceva).

RX(14) OF 57



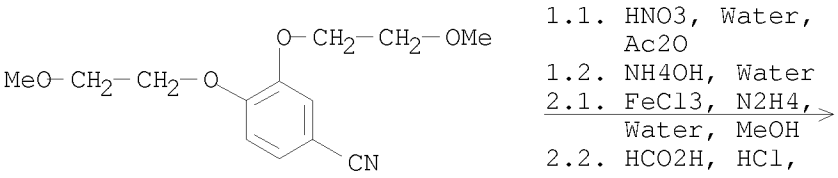
(step 1)



81%

NOTE: key intermediate
CON: STAGE(1) 1 hour, reflux; 2 hours, reflux
STAGE(2) room temperature -> 130 deg C; 3 hours, 130 deg C

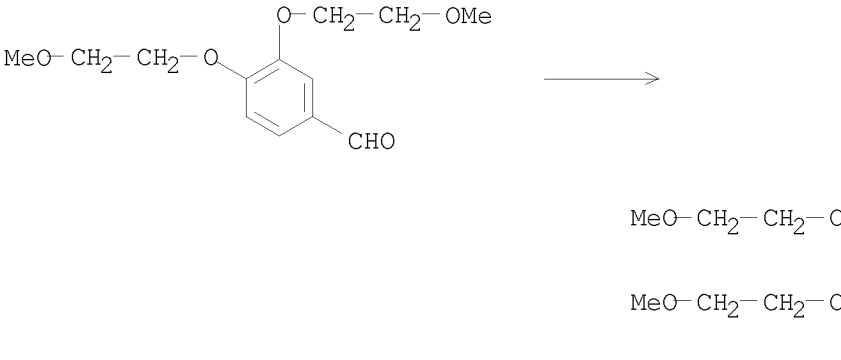
RX(37) OF 57 - 2 STEPS



81%

NOTE: 1) 75% overall yield from 3,4-dihydroxybenzaldehyde, regioselective, 2) key intermediate
CON: STEP(1.1) 45 - 50 deg C; 8 hours, 45 - 50 deg C
STEP(1.2) pH 8
STEP(2.1) 1 hour, reflux; 2 hours, reflux
STEP(2.2) room temperature -> 130 deg C; 3 hours, 130 deg C

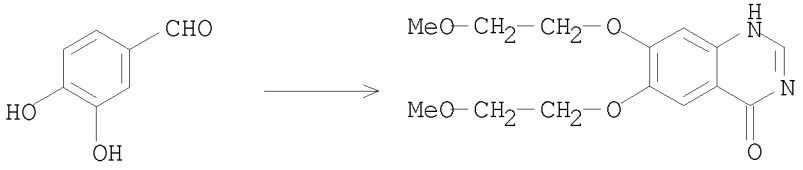
RX(48) OF 57 - 3 STEPS



81%

NOTE: 2) 75% overall yield from 3,4-dihydroxybenzaldehyde, regioselective, 3) key intermediate
CON: STEP(1.1) 25 deg C -> reflux; 1 hour, reflux
STEP(1.2) room temperature -> 110 deg C; 3 hours, 110 deg C
STEP(1.3) pH 8
STEP(2.1) 45 - 50 deg C; 8 hours, 45 - 50 deg C
STEP(2.2) pH 8
STEP(3.1) 1 hour, reflux; 2 hours, reflux
STEP(3.2) room temperature -> 130 deg C; 3 hours, 130 deg C

RX(49) OF 57 - 4 STEPS

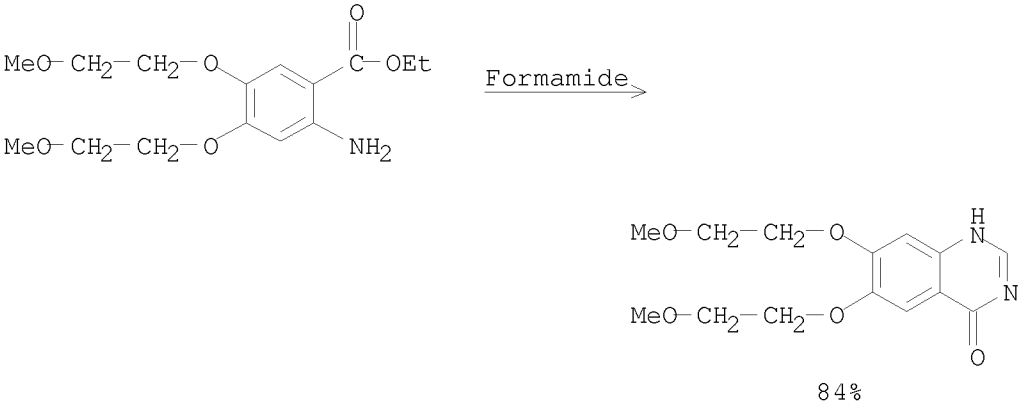


81%

NOTE: 3) 75% overall yield from 3,4-dihydroxybenzaldehyde, regioselective, 4) key intermediate
CON: STEP(1.1) room temperature -> 100 deg C; 3 hours, 100 deg C
STEP(2.1) 25 deg C -> reflux; 1 hour, reflux
STEP(2.2) room temperature -> 110 deg C; 3 hours, 110 deg C
STEP(2.3) pH 8
STEP(3.1) 45 - 50 deg C; 8 hours, 45 - 50 deg C
STEP(3.2) pH 8
STEP(4.1) 1 hour, reflux; 2 hours, reflux
STEP(4.2) room temperature -> 130 deg C; 3 hours, 130 deg C

L3 ANSWER 2 OF 10 CASREACT COPYRIGHT 2008 ACS on STN
146:274315 Improved synthesis of substituted 6,7-dihydroxy-4-quinazolineamines: tandutinib, erlotinib and gefitinib. Knesl, Petr; Roeseling, Dirk; Jordis, Ulrich (Institute of Applied Synthetic Chemistry, Vienna University of Technology, Vienna, 1060, Austria). Molecules, 11(4), 286-297 (English) 2006. CODEN: MOLEFW. ISSN: 1420-3049. URL: http://www.mdpi.org/molecules/papers/11040286.pdf Publisher: Molecular Diversity Preservation International.
AB The synthesis of three substituted 6,7-dihydroxy-4-quinazolineamines: tandutinib, erlotinib and gefitinib in improved yields is reported. The intermediates were characterized by NMR and the purities determined by HPLC.

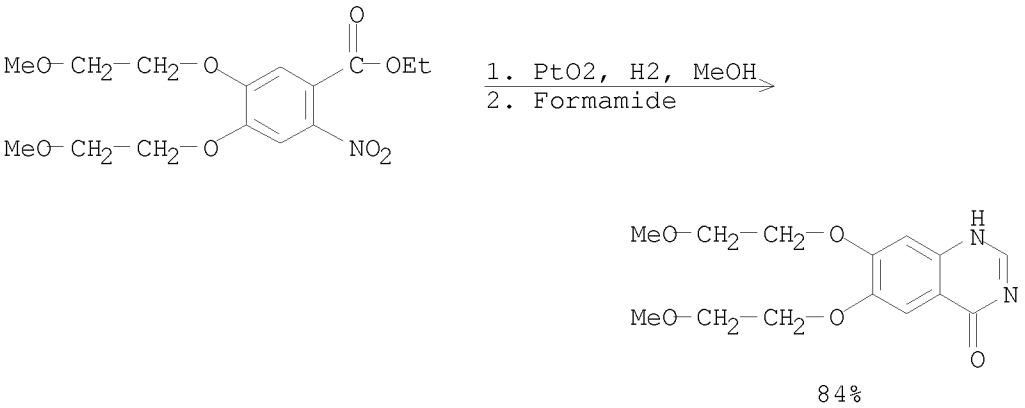
RX(12) OF 81



84%

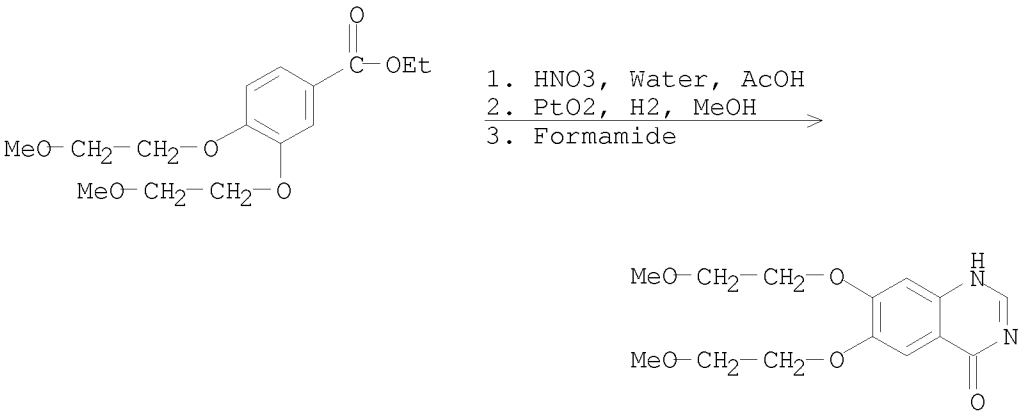
CON: 12 hours, 165 - 170 deg C

RX(32) OF 81 - 2 STEPS



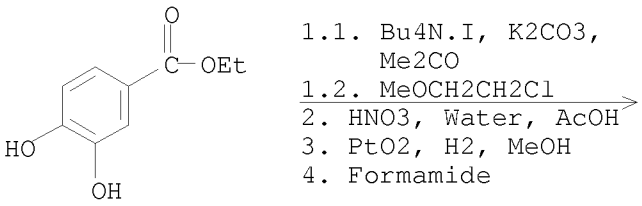
CON: STEP(1) room temperature, 50 psi
STEP(2) 12 hours, 165 - 170 deg C

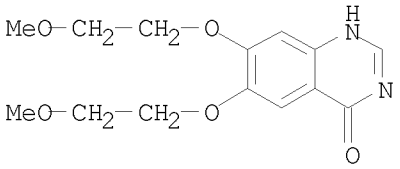
RX(53) OF 81 - 3 STEPS



CON: STEP(1.1) 30 minutes, 0 - 5 deg C; 24 hours, room temperature
STEP(2) room temperature, 50 psi
STEP(3) 12 hours, 165 - 170 deg C

RX(54) OF 81 - 4 STEPS





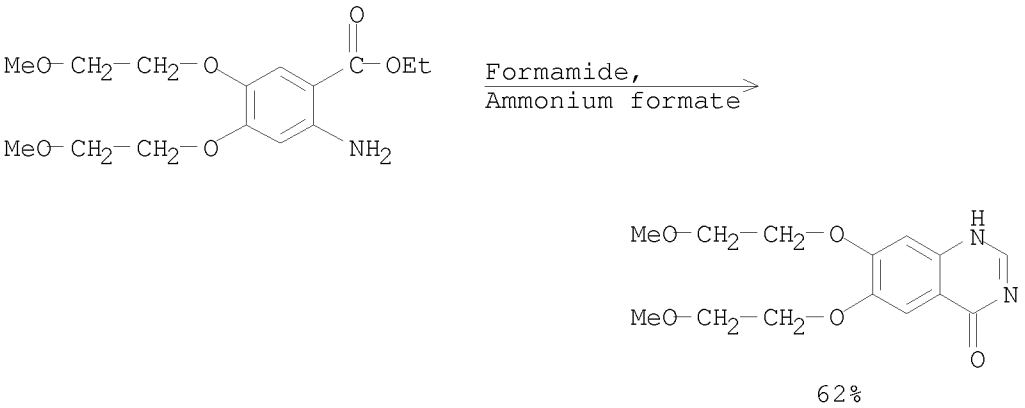
84%

NOTE: 1) alternative preparation shown
CON: STEP(1.1) 20 minutes, room temperature
STEP(1.2) 5 days, reflux
STEP(2.1) 30 minutes, 0 - 5 deg C; 24 hours, room temperature
STEP(3) room temperature, 50 psi
STEP(4) 12 hours, 165 - 170 deg C

L3 ANSWER 3 OF 10 CASREACT COPYRIGHT 2008 ACS on STN
145:271722 Fluorine-18 labeling of 6,7-disubstituted anilinoquinazoline derivatives for positron emission tomography (PET) imaging of tyrosine kinase receptors: Synthesis of 18F-Iressa and related molecular probes. Seimbille, Yann; Phelps, Michael E.; Czernin, Johannes; Silverman, Daniel H. S. (Ahmanson Biological Imaging Division, Department of Molecular and Medical Pharmacology, University of California, Los Angeles, CA, 90095-6942, USA). Journal of Labelled Compounds & Radiopharmaceuticals, 48(11), 829-843 (English) 2005. CODEN: JLCRD4. ISSN: 0362-4803. Publisher: John Wiley & Sons Ltd..

AB Inhibitors of tyrosine kinase enzymic activity are a promising new class of antineoplastic agents. Although clin. studies performed over the last decade give more insight on the potential therapeutic applications of such drugs, identification of the individual patients who might benefit from them remains a major challenge. The authors have developed a synthetic strategy for the production of a wide variety of radiolabeled 6,7-disubstituted 4-anilinoquinazolines suitable for non-invasive imaging of tyrosine kinase receptors to predict therapy effectiveness. Three new F-18 labeled radiopharmaceuticals based on the therapeutic agents Tarceva, Iressa, and ZD6474 were synthesized. Decay-corrected yields were 25-40% for a total synthesis time of 120 min, thus providing F-18 labeled tyrosine kinase inhibitors in quantities and times practical for use as PET radiopharmaceuticals.

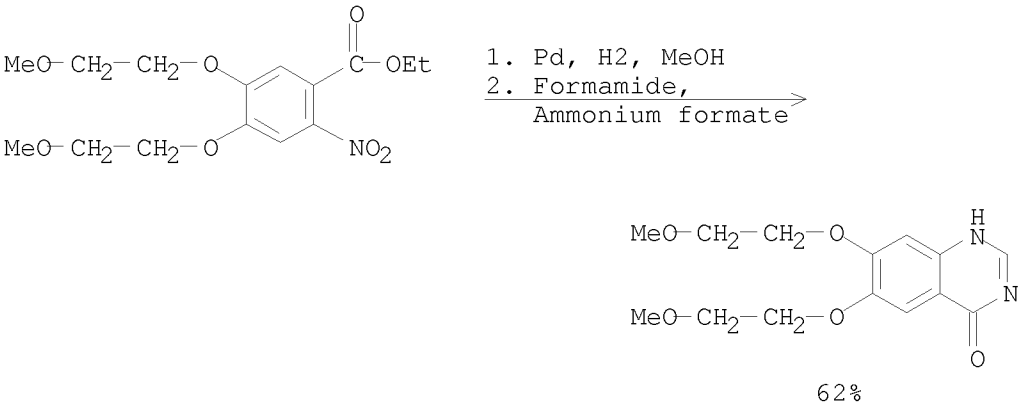
RX(23) OF 163



62%

NOTE: Niementowski condensation
CON: 3 hours, 160 deg C

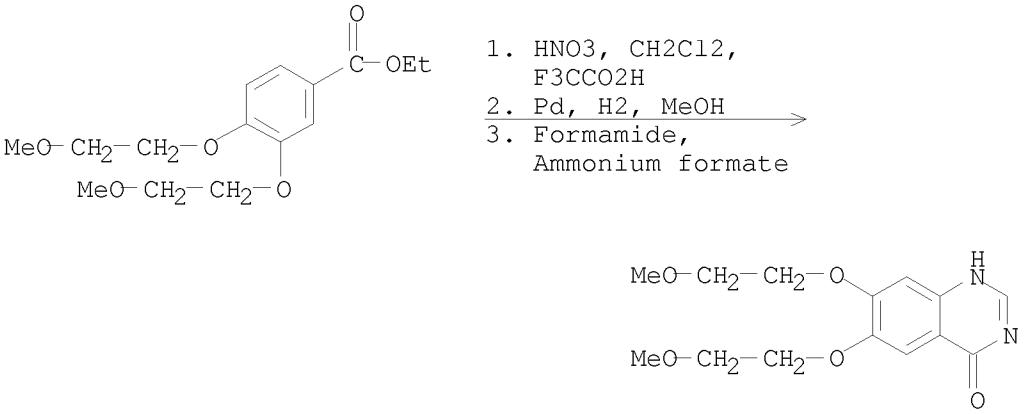
RX(45) OF 163 - 2 STEPS



62%

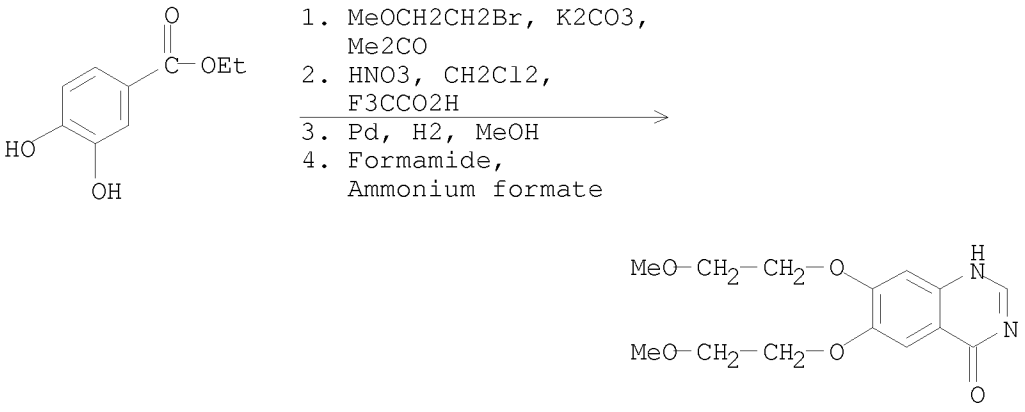
NOTE: 2) Niementowski condensation
CON: STEP(1) room temperature
STEP(2) 3 hours, 160 deg C

RX(74) OF 163 - 3 STEPS



NOTE: 3) Niementowski condensation
CON: STEP(1.1) 15 minutes, 0 - 5 deg C; 2 hours, room temperature
STEP(2) room temperature
STEP(3) 3 hours, 160 deg C

RX(75) OF 163 - 4 STEPS

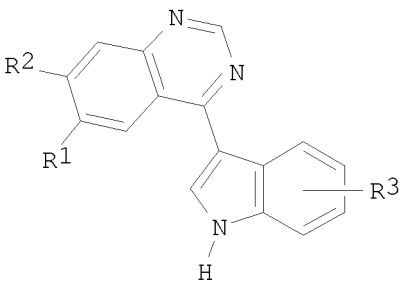


NOTE: 4) Niementowski condensation
CON: STEP(1) 72 hours, reflux
STEP(2.1) 15 minutes, 0 - 5 deg C; 2 hours, room temperature
STEP(3) room temperature
STEP(4) 3 hours, 160 deg C

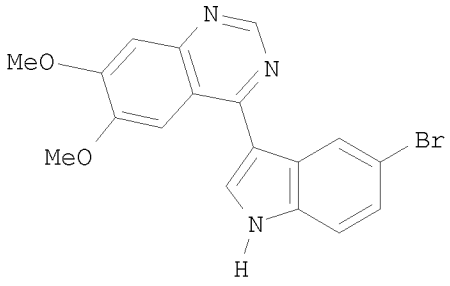
L3 ANSWER 4 OF 10 CASREACT COPYRIGHT 2008 ACS on STN
145:249220 Preparation of 4-(indol-3-yl)quinazolines as epidermal growth factor receptor inhibitors. Loewe, Werner; Lueth, Anja (Freie Universitaet Berlin, Germany). PCT Int. Appl. WO 2006084882 A2 20060817, 23pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA; RW: AT,

BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IS, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (German). CODEN: PIXXD2. APPLICATION: WO 2006-EP50813 20060209. PRIORITY: DE 2005-102005007151 20050211.

GI



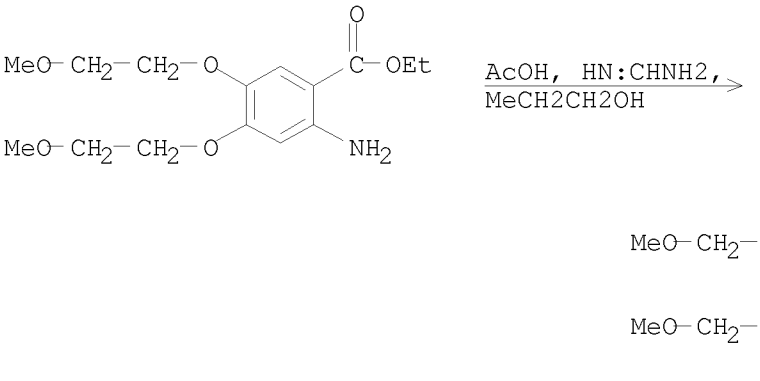
I



II

AB Title compds. I [R1 = methoxy, ethoxy, propoxy, etc.; R2 = H, methoxy, ethoxy, etc.; R3 = (R3')n; R3' = halo, halo substituted benzyloxyl, alkyl, etc.; n = 1-3] and their pharmaceutically acceptable salts were prepared For example, Mg mediated coupling of 4-chloro-6,7-dimethoxyquinazoline and 5-bromoindole afforded quinazoline II. In epidermal growth factor receptor inhibition assays, 4-examples of compds. I exhibited 61-81% inhibition at 0.1 μM.

RX(5) OF 18



CON: 24 hours, reflux

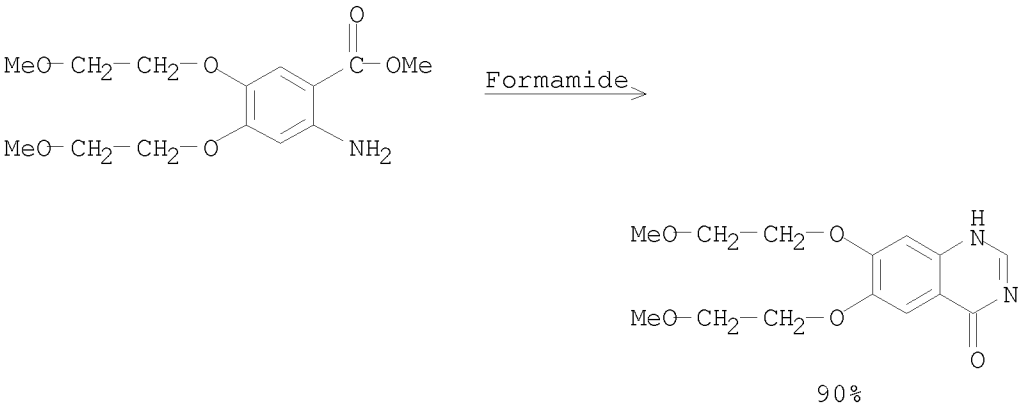
L3 ANSWER 5 OF 10 CASREACT COPYRIGHT 2008 ACS on STN

144:370039 Synthesis and biological evaluation of allenic quinazolines using palladium-catalyzed hydride-transfer reaction. Nakamura, Hiroyuki; Onagi, Shinya (Department of Chemistry, Faculty of Science, Gakushuin University, Mejiro, Tokyo, 171-8588, Japan). Tetrahedron Letters, 47(15), 2539-2542 (English) 2006. CODEN: TELEAY. ISSN: 0040-4039. Publisher: Elsevier B.V..

AB Allenic quinazolines were designed as mimics of Tarceva, which is an epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor, and synthesized from the corresponding 4-(iodoanilino)quinazolines or 4-(iodophenoxy)quinazolines with N,N-dicyclohexylprop-2-ynylamine by the Sonogashira coupling followed by palladium-catalyzed hydride-transfer

reaction. Cell growth inhibition of the new compds. toward A431, Kato III, SKBR3, and HepG2 was examined One of the compds. synthesized, showed a similar cell growth inhibition to Tarceva. Moreover, two other compds. exhibited a specific growth inhibition toward Kato III cells (IC50 = 12 and 4.7 μM, resp.), although a significant inhibition toward other three cell lines was not observed at a 100 μM concentration of compds.

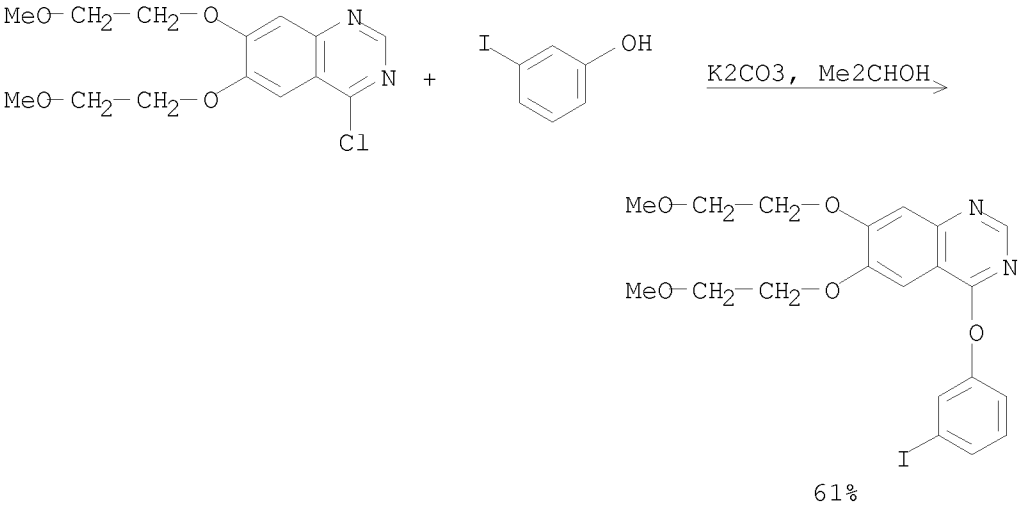
RX(16) OF 171



90%

CON: 160 deg C

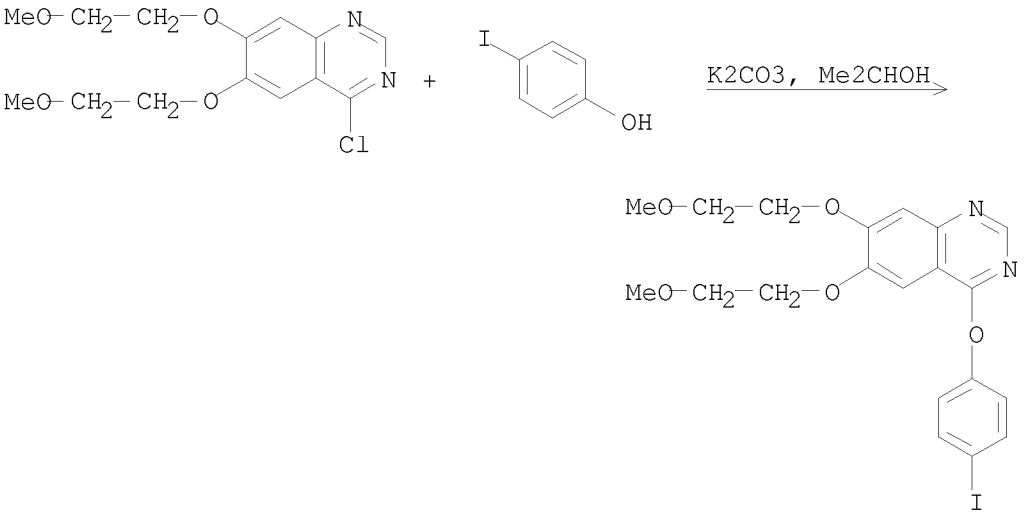
RX(20) OF 171



61%

CON: reflux

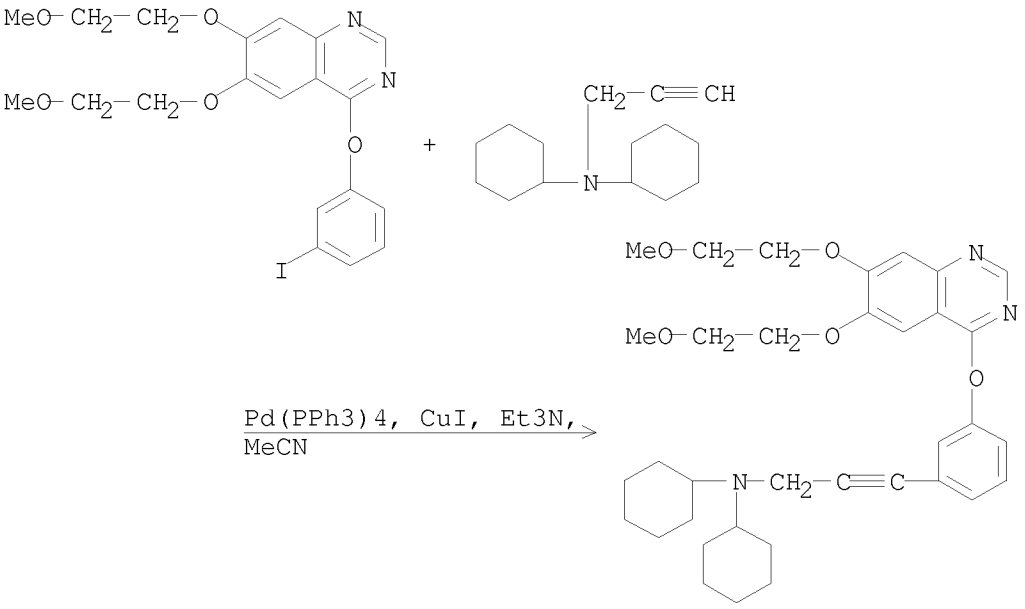
RX(21) OF 171



99%

CON: reflux

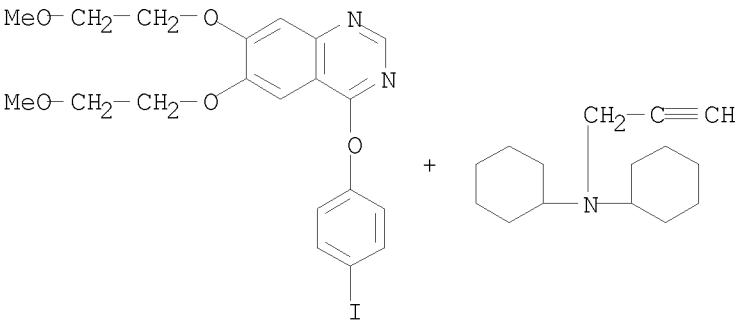
RX(24) OF 171



24%

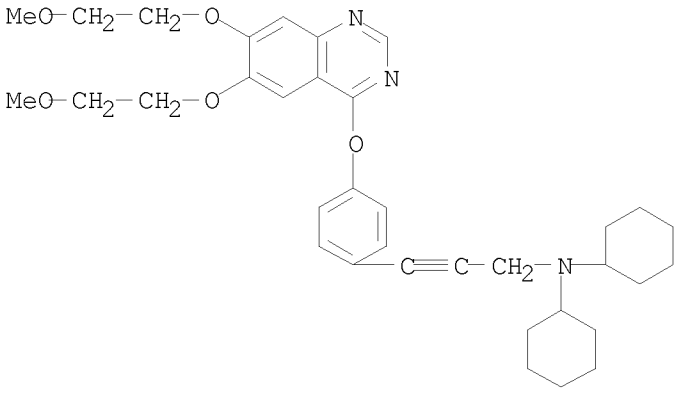
CON: 60 deg C

RX(25) OF 171



Pd(PPh3)4, CuI, Et3N, MeCN

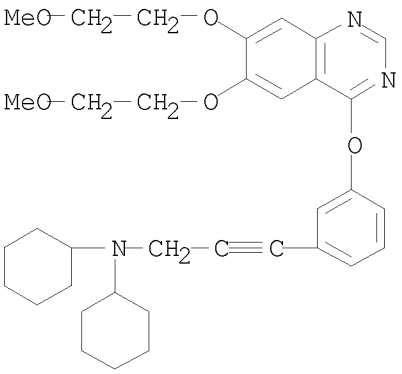
RX(25) OF 171



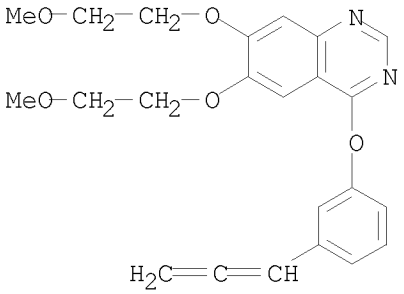
60%

CON: 60 deg C

RX(32) OF 171



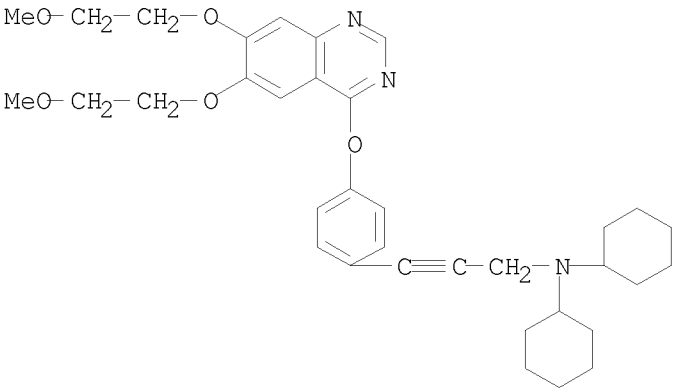
Pd complex,
R:76858-94-1, CHCl3



55%

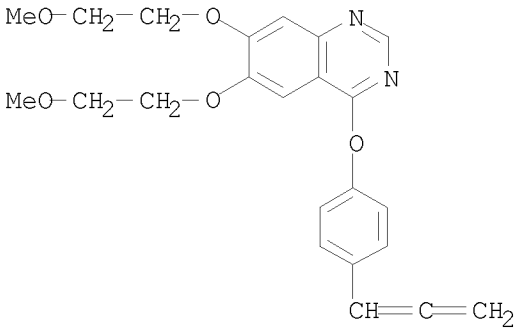
CON: 100 deg C

RX(33) OF 171



Pd complex,
R:76858-94-1, CHCl3

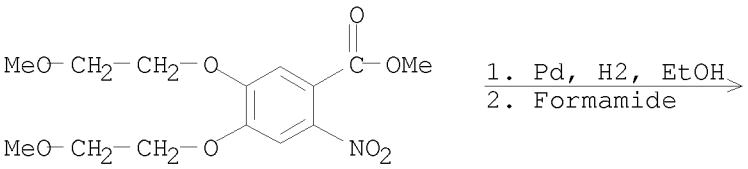
RX(33) OF 171

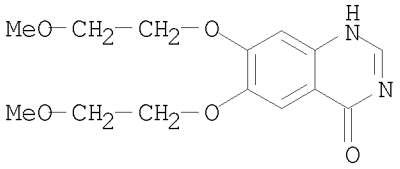


61%

CON: 100 deg C

RX(51) OF 171 - 2 STEPS

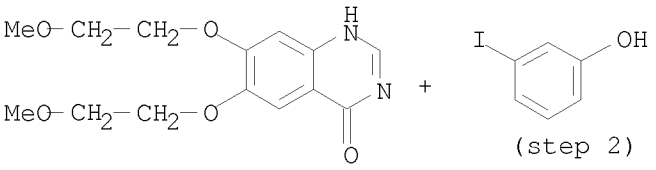




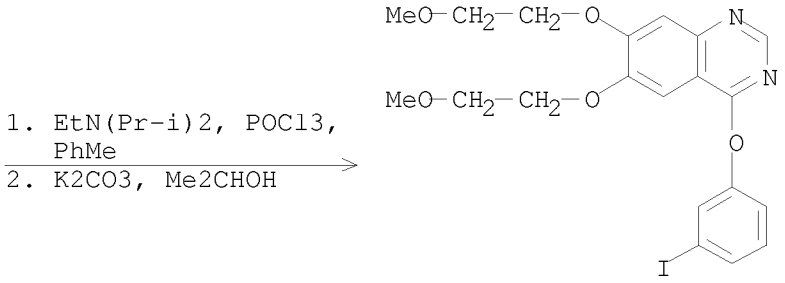
90%

CON: STEP(2) 160 deg C

RX(55) OF 171 - 2 STEPS



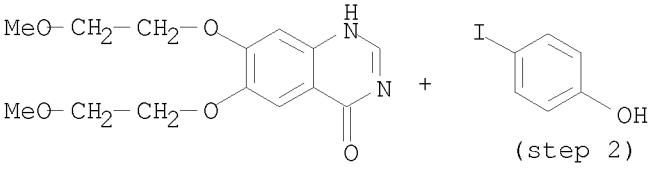
(step 2)



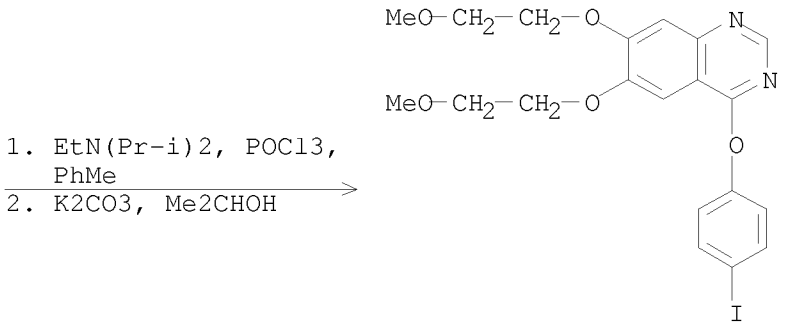
61%

CON: STEP(1) reflux
STEP(2) reflux

RX(56) OF 171 - 2 STEPS



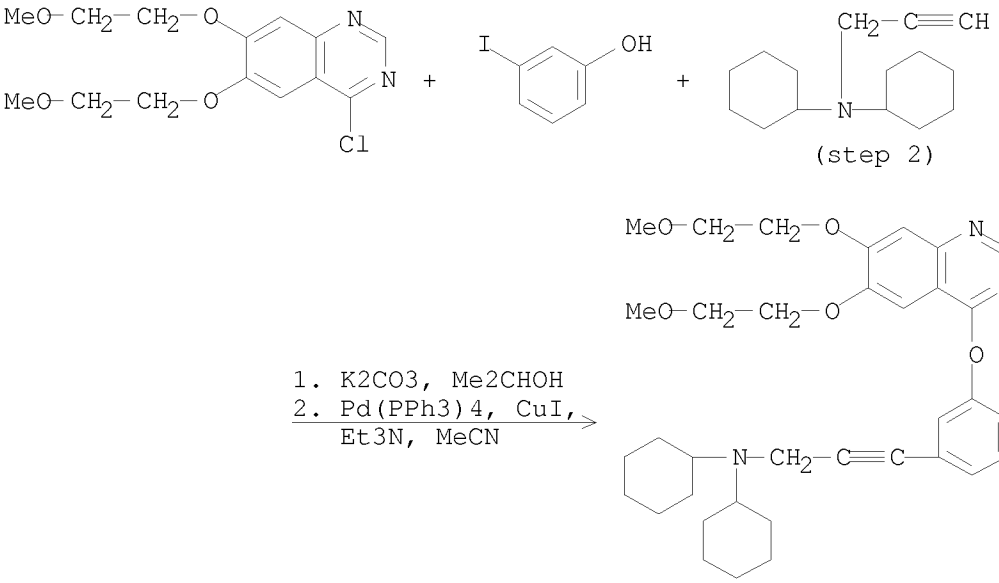
(step 2)



99%

CON: STEP(1) reflux
STEP(2) reflux

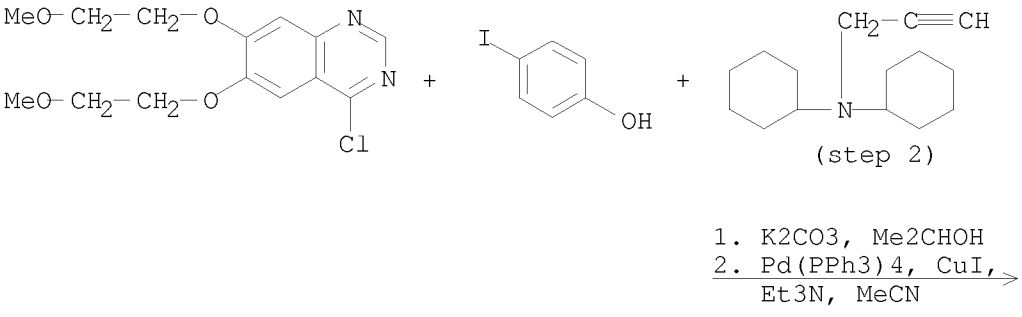
RX(59) OF 171 - 2 STEPS



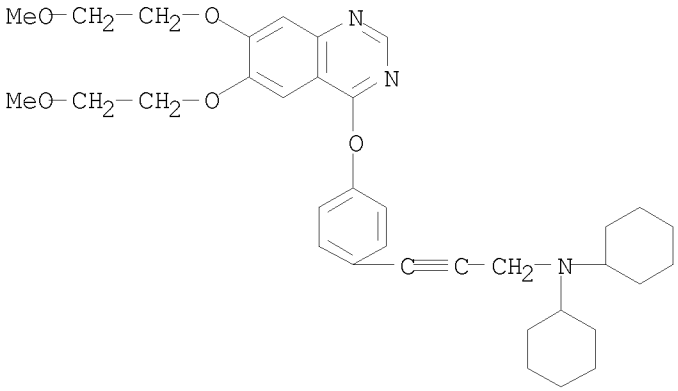
24%

CON: STEP(1) reflux
STEP(2) 60 deg C

RX(60) OF 171 - 2 STEPS



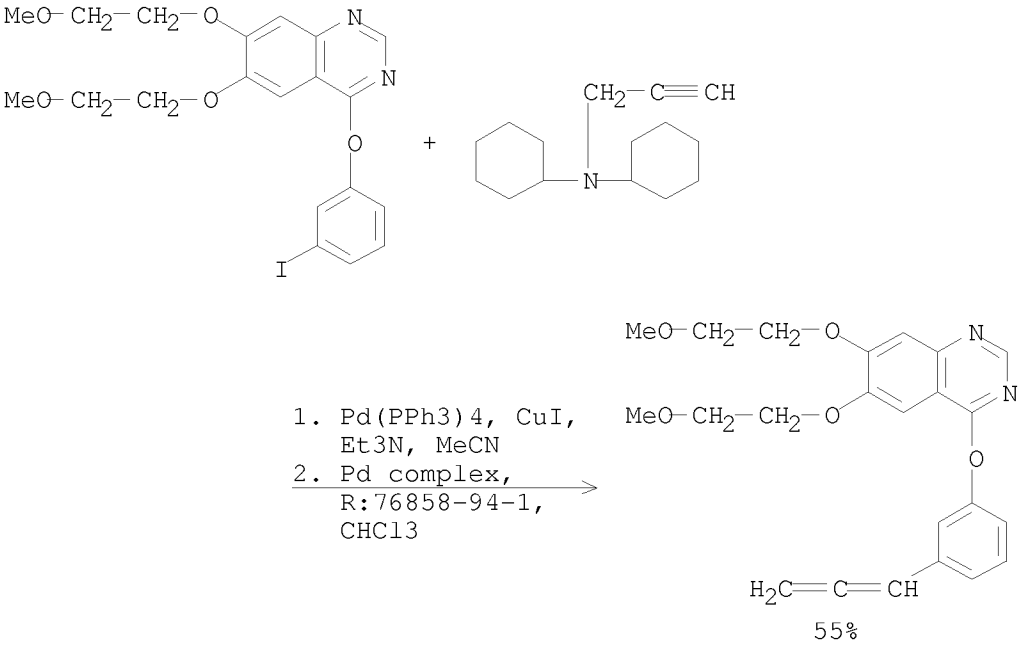
RX(60) OF 171 - 2 STEPS



60%

CON: STEP(1) reflux
STEP(2) 60 deg C

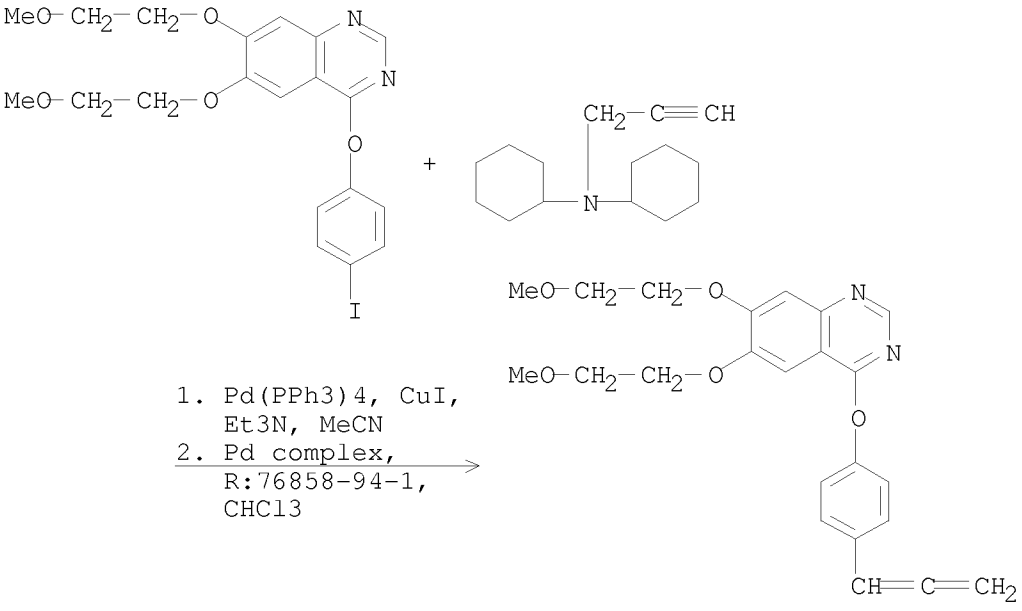
RX(63) OF 171 - 2 STEPS



55%

CON: STEP(1) 60 deg C
STEP(2) 100 deg C

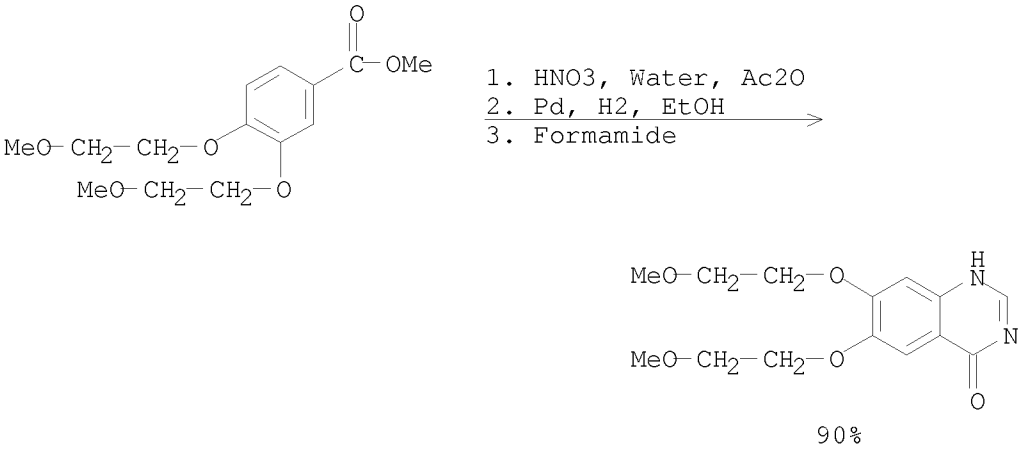
RX(64) OF 171 - 2 STEPS



61%

CON: STEP(1) 60 deg C
STEP(2) 100 deg C

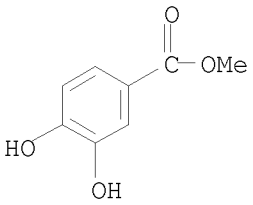
RX(89) OF 171 - 3 STEPS



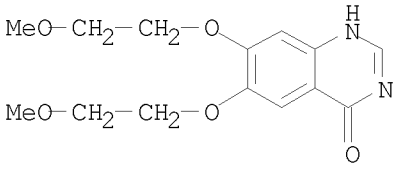
90%

CON: STEP(3) 160 deg C

RX(90) OF 171 - 4 STEPS



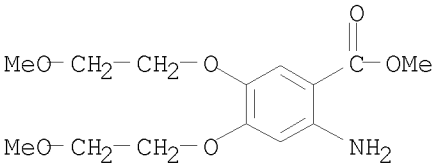
1. MeOCH2CH2Br, K2CO3, Me2CO, Bu4N.I
2. HNO3, Water, Ac2O
3. Pd, H2, EtOH
4. Formamide



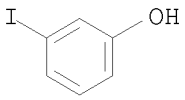
90%

CON: STEP(1) reflux
STEP(4) 160 deg C

RX(95) OF 171 - 3 STEPS

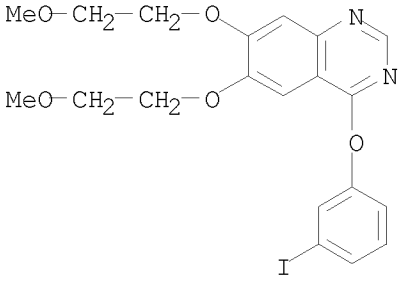


+



(step 3)

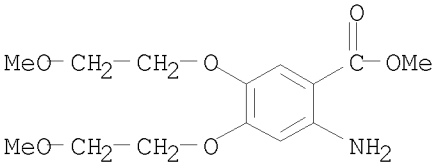
1. Formamide
2. EtN(Pr-i)2, POCl3, PhMe
3. K2CO3, Me2CHOH



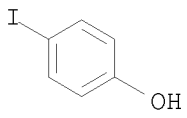
61%

CON: STEP(1) 160 deg C
STEP(2) reflux
STEP(3) reflux

RX(96) OF 171 - 3 STEPS

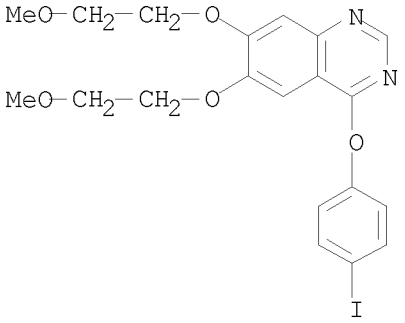


+



(step 3)

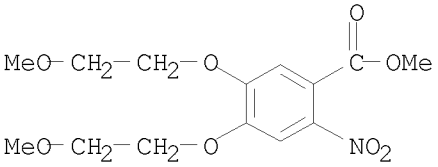
1. Formamide
2. EtN(Pr-i)2, POCl3, PhMe
3. K2CO3, Me2CHOH



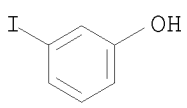
99%

CON: STEP(1) 160 deg C
STEP(2) reflux
STEP(3) reflux

RX(99) OF 171 - 4 STEPS

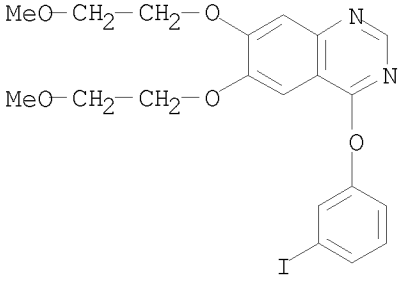


+



(step 4)

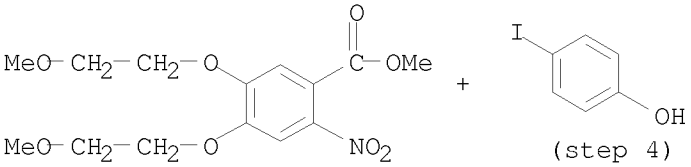
1. Pd, H2, EtOH
2. Formamide
3. EtN(Pr-i)2, POCl3, PhMe
4. K2CO3, Me2CHOH



61%

CON: STEP(2) 160 deg C
STEP(3) reflux
STEP(4) reflux

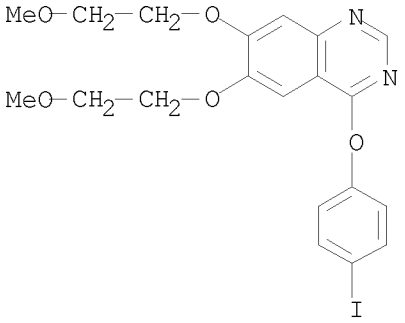
RX(100) OF 171 - 4 STEPS



+

(step 4)

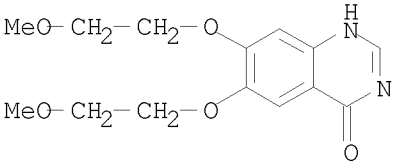
1. Pd, H2, EtOH
2. Formamide
3. EtN(Pr-i)2, POCl3, PhMe
4. K2CO3, Me2CHOH



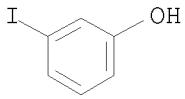
99%

CON: STEP(2) 160 deg C
STEP(3) reflux
STEP(4) reflux

RX(103) OF 171 - 3 STEPS

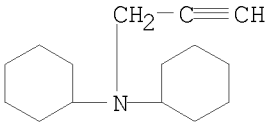


+



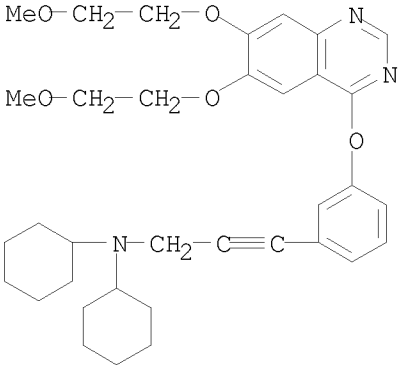
(step 2)

+



(step 3)

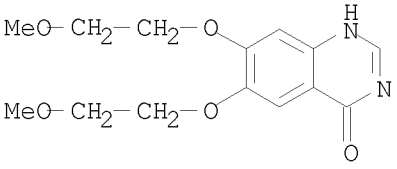
1. EtN(Pr-i)2, POCl3, PhMe
2. K2CO3, Me2CHOH
3. Pd(PPh3)4, CuI, Et3N, MeCN



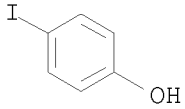
24%

CON: STEP(1) reflux
STEP(2) reflux
STEP(3) 60 deg C

RX(104) OF 171 - 3 STEPS

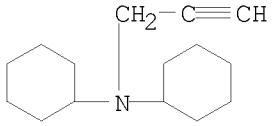


+



(step 2)

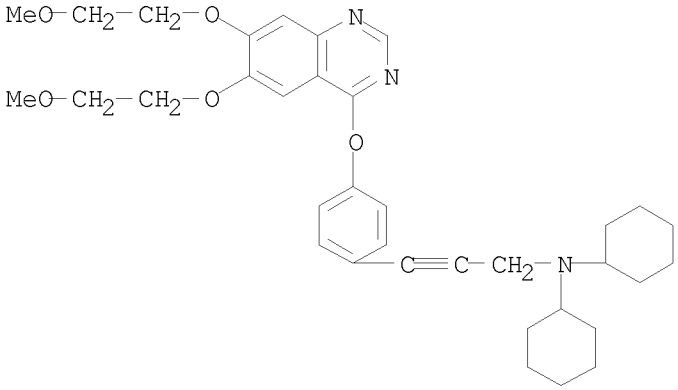
+



(step 3)

1. EtN(Pr-i)2, POCl3, PhMe
2. K2CO3, Me2CHOH
3. Pd(PPh3)4, CuI, Et3N, MeCN

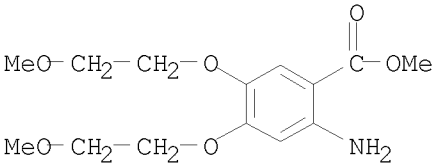
RX(104) OF 171 - 3 STEPS



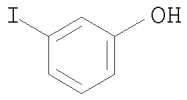
60%

CON: STEP(1) reflux
STEP(2) reflux
STEP(3) 60 deg C

RX(107) OF 171 - 4 STEPS

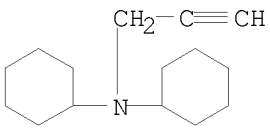


+



(step 3)

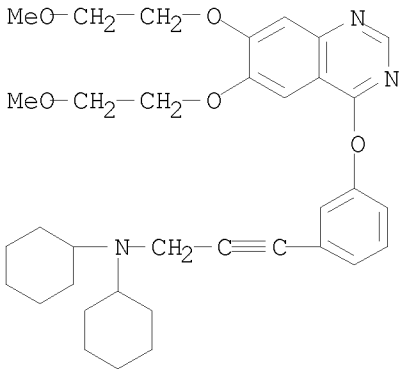
+



(step 4)

1. Formamide
2. EtN(Pr-i)2, POCl3, PhMe
3. K2CO3, Me2CHOH
4. Pd(PPh3)4, CuI, Et3N, MeCN

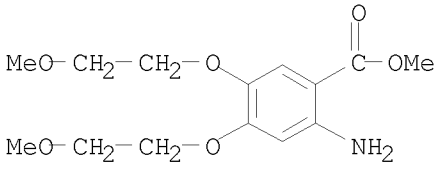
RX(107) OF 171 - 4 STEPS



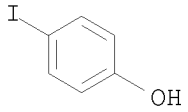
24%

CON: STEP(1) 160 deg C
STEP(2) reflux
STEP(3) reflux
STEP(4) 60 deg C

RX(108) OF 171 - 4 STEPS

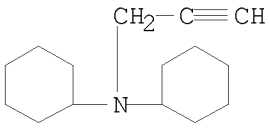


+



(step 3)

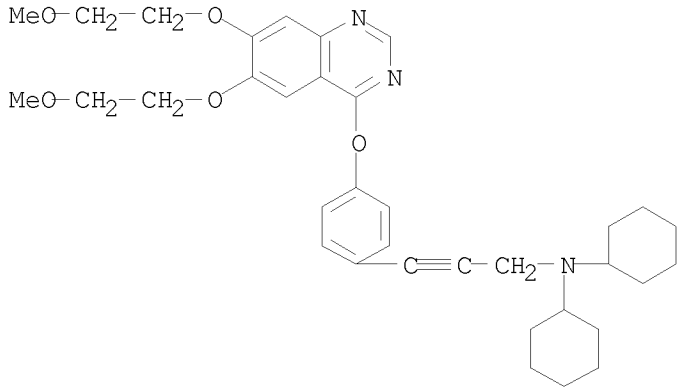
+



(step 4)

1. Formamide
2. EtN(Pr-i)2, POCl3, PhMe
3. K2CO3, Me2CHOH
4. Pd(PPh3)4, CuI, Et3N, MeCN

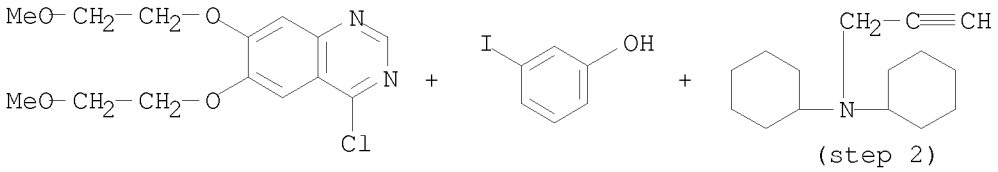
RX(108) OF 171 - 4 STEPS



60%

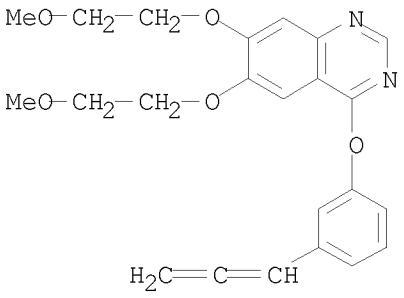
CON: STEP(1) 160 deg C
STEP(2) reflux
STEP(3) reflux
STEP(4) 60 deg C

RX(113) OF 171 - 3 STEPS



(step 2)

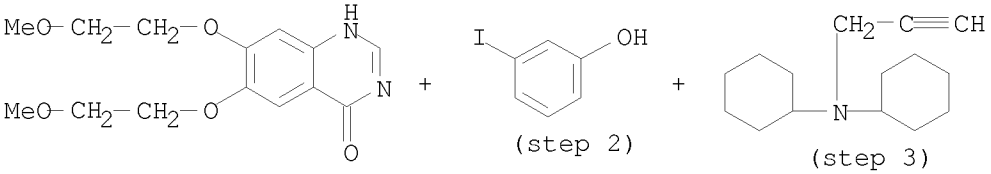
1. K2CO3, Me2CHOH
2. Pd(PPh3)4, CuI, Et3N, MeCN
3. Pd complex, R:76858-94-1, CHCl3



55%

CON: STEP(1) reflux
STEP(2) 60 deg C
STEP(3) 100 deg C

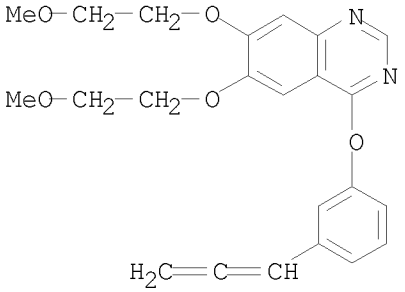
RX(114) OF 171 - 4 STEPS



(step 2)

(step 3)

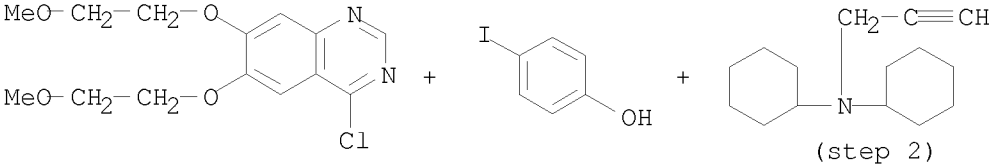
1. EtN(Pr-i)2, POCl3, PhMe
2. K2CO3, Me2CHOH
3. Pd(PPh3)4, CuI, Et3N, MeCN
4. Pd complex, R:76858-94-1, CHCl3



55%

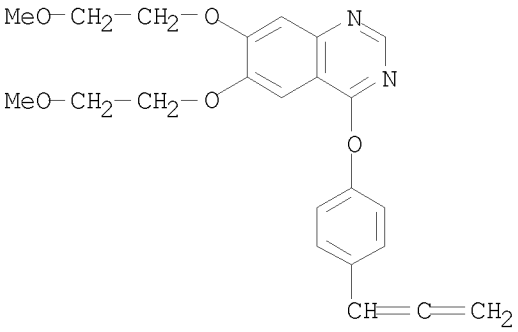
CON: STEP(1) reflux
STEP(2) reflux
STEP(3) 60 deg C
STEP(4) 100 deg C

RX(115) OF 171 - 3 STEPS



(step 2)

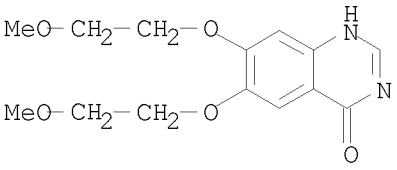
1. K2CO3, Me2CHOH
2. Pd(PPh3)4, CuI, Et3N, MeCN
3. Pd complex, R:76858-94-1, CHCl3



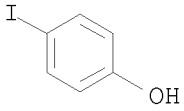
61%

CON: STEP(1) reflux
STEP(2) 60 deg C
STEP(3) 100 deg C

RX(116) OF 171 - 4 STEPS

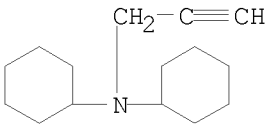


+



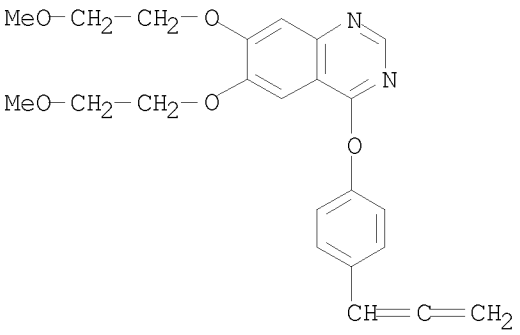
(step 2)

+



(step 3)

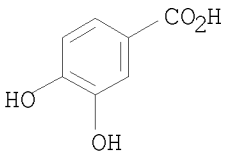
1. EtN(Pr-i)2, POCl3, PhMe
2. K2CO3, Me2CHOH
3. Pd(PPh3)4, CuI, Et3N, MeCN
4. Pd complex, R:76858-94-1, CHCl3



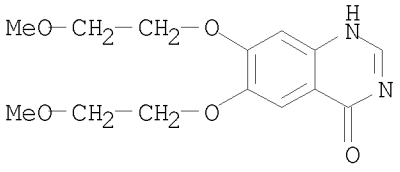
61%

CON: STEP(1) reflux
STEP(2) reflux
STEP(3) 60 deg C
STEP(4) 100 deg C

RX(121) OF 171 - 5 STEPS



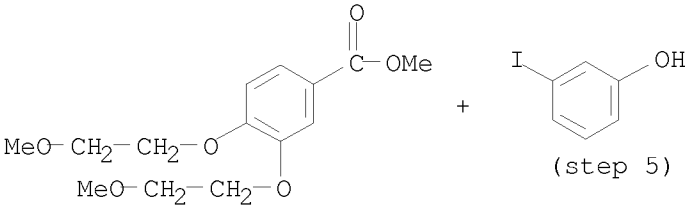
1. MeOH, H2SO4
2. MeOCH2CH2Br, K2CO3, Me2CO, Bu4N.I
3. HNO3, Water, Ac2O
4. Pd, H2, EtOH
5. Formamide



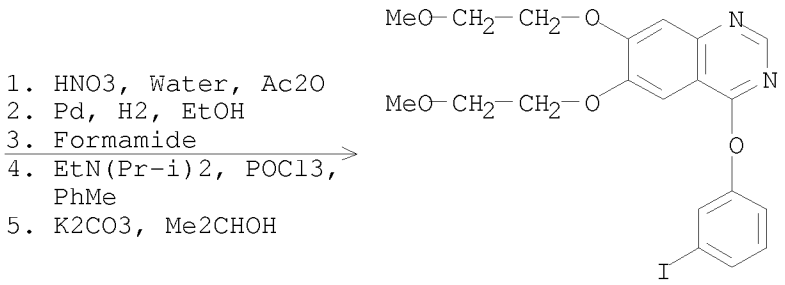
90%

CON: STEP(1) reflux
STEP(2) reflux
STEP(5) 160 deg C

RX(126) OF 171 - 5 STEPS



(step 5)

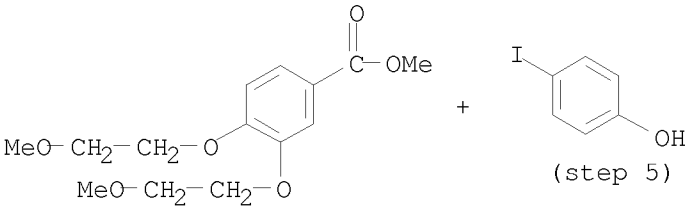


1. HNO3, Water, Ac2O
2. Pd, H2, EtOH
3. Formamide
4. EtN(Pr-i)2, POCl3, PhMe
5. K2CO3, Me2CHOH

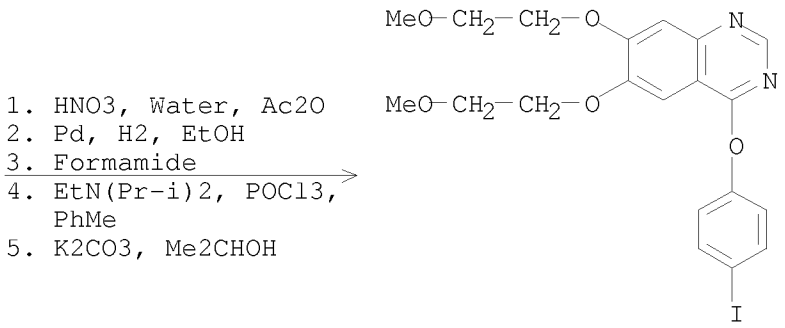
61%

CON: STEP(3) 160 deg C
STEP(4) reflux
STEP(5) reflux

RX(127) OF 171 - 5 STEPS



(step 5)

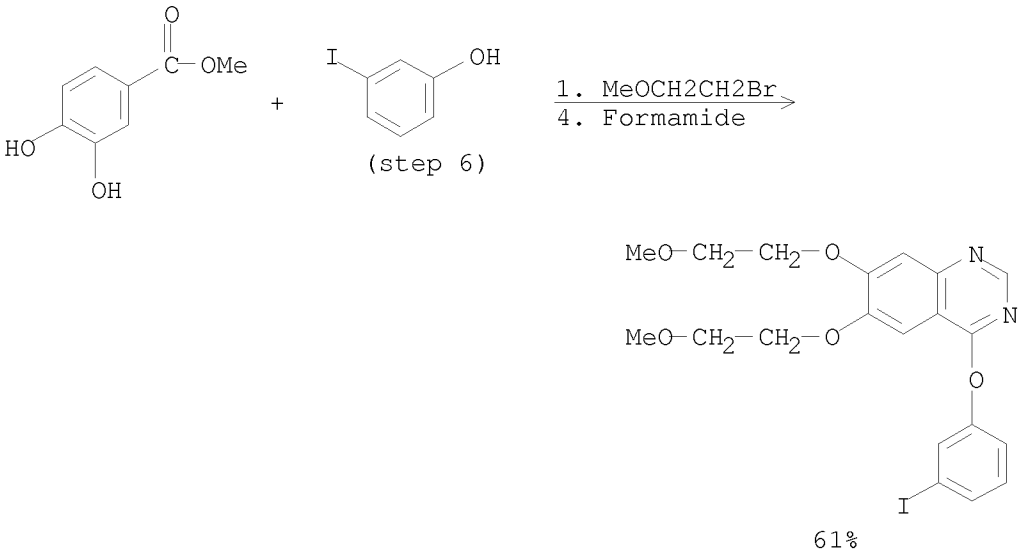


1. HNO3, Water, Ac2O
2. Pd, H2, EtOH
3. Formamide
4. EtN(Pr-i)2, POCl3, PhMe
5. K2CO3, Me2CHOH

99%

CON: STEP(3) 160 deg C
STEP(4) reflux
STEP(5) reflux

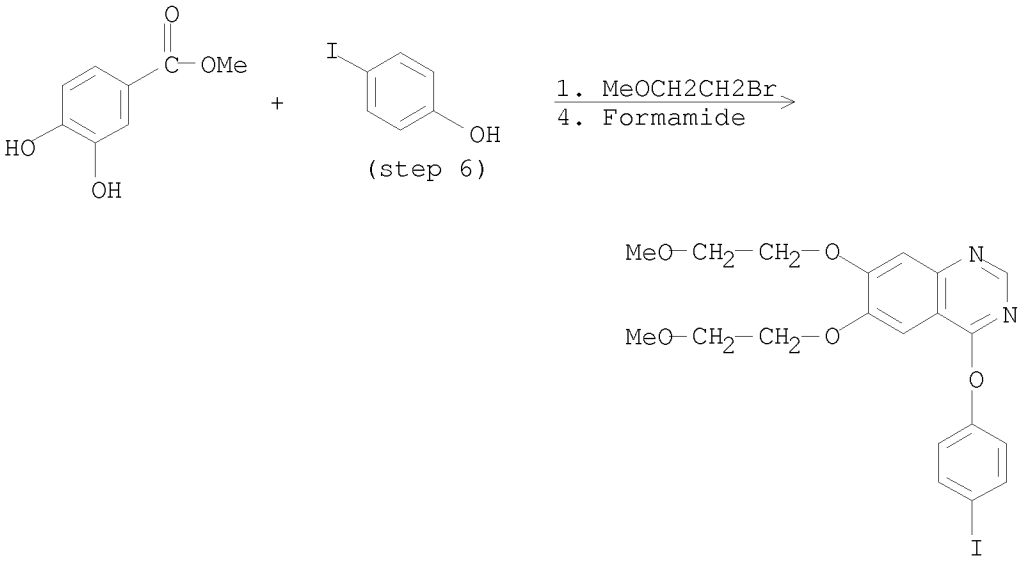
RX(130) OF 171 - 6 STEPS



61%

CON: STEP(1) reflux
STEP(4) 160 deg C
STEP(5) reflux
STEP(6) reflux

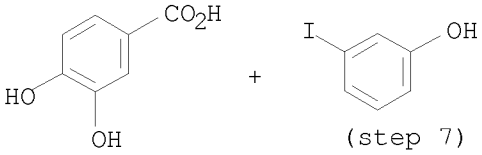
RX(131) OF 171 - 6 STEPS



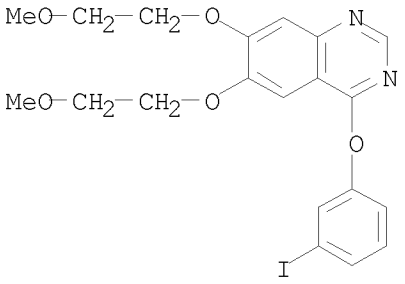
99%

CON: STEP(1) reflux
STEP(4) 160 deg C
STEP(5) reflux
STEP(6) reflux

RX(134) OF 171 - 7 STEPS



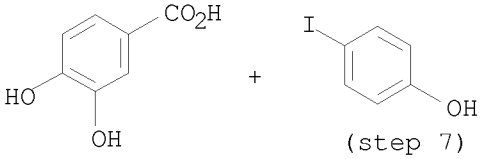
1. MeOH
2. MeOCH2CH2Br
5. Formamide



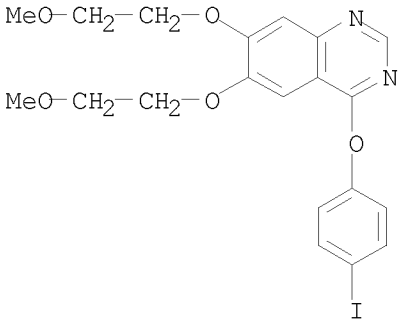
61%

CON: STEP(1) reflux
STEP(2) reflux
STEP(5) 160 deg C
STEP(6) reflux
STEP(7) reflux

RX(135) OF 171 - 7 STEPS



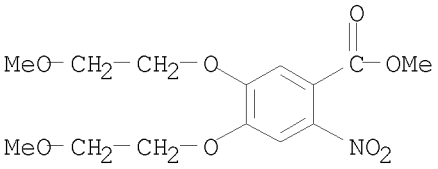
1. MeOH
2. MeOCH2CH2Br
5. Formamide



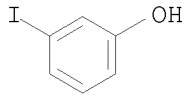
99%

CON: STEP(1) reflux
STEP(2) reflux
STEP(5) 160 deg C
STEP(6) reflux
STEP(7) reflux

RX(138) OF 171 - 5 STEPS

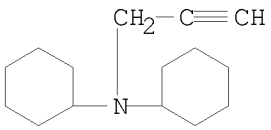


+



(step 4)

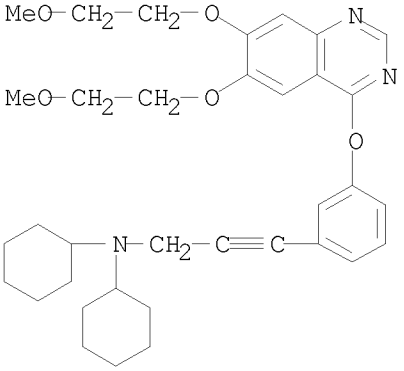
+



(step 5)

1. Pd, H2, EtOH
2. Formamide
3. EtN(Pr-i)2, POCl3, PhMe
4. K2CO3, Me2CHOH
5. Pd(PPh3)4, CuI, Et3N, MeCN

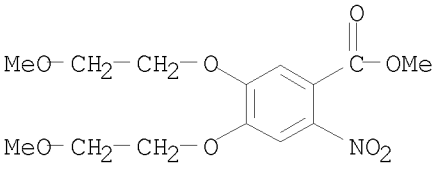
RX(138) OF 171 - 5 STEPS



24%

CON: STEP(2) 160 deg C
STEP(3) reflux
STEP(4) reflux
STEP(5) 60 deg C

RX(139) OF 171 - 5 STEPS



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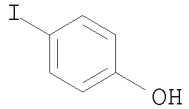
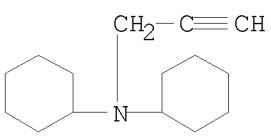


(step 4)

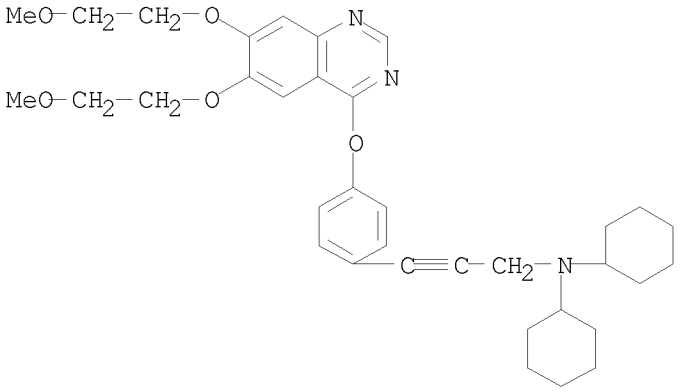
+



(step 5)

1. Pd, H2, EtOH
2. Formamide
3. EtN(Pr-i)2, POCl3, PhMe
4. K2CO3, Me2CHOH
5. Pd(PPh3)4, CuI, Et3N, MeCN

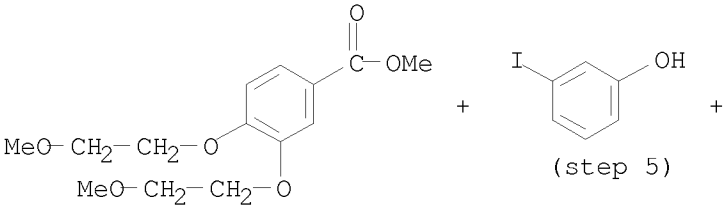
RX(139) OF 171 - 5 STEPS



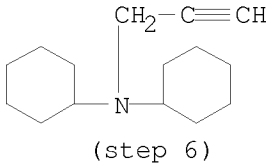
60%

CON: STEP(2) 160 deg C
STEP(3) reflux
STEP(4) reflux
STEP(5) 60 deg C

RX(142) OF 171 - 6 STEPS

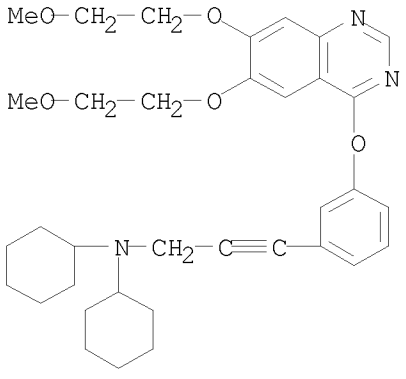


(step 5)



(step 6)

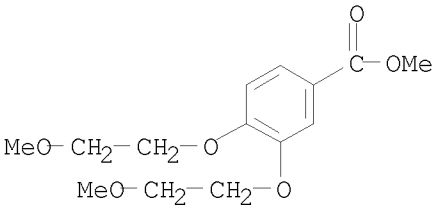
3. Formamide



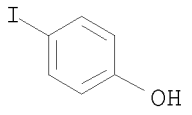
24%

CON: STEP(3) 160 deg C
STEP(4) reflux
STEP(5) reflux
STEP(6) 60 deg C

RX(143) OF 171 - 6 STEPS

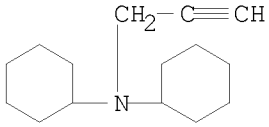


+



+

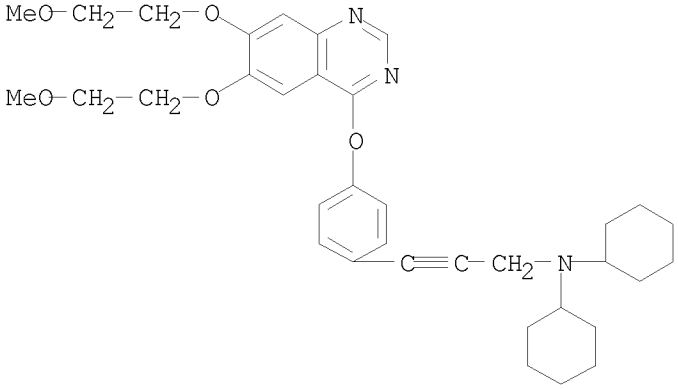
(step 5)



(step 6)

3. Formamide

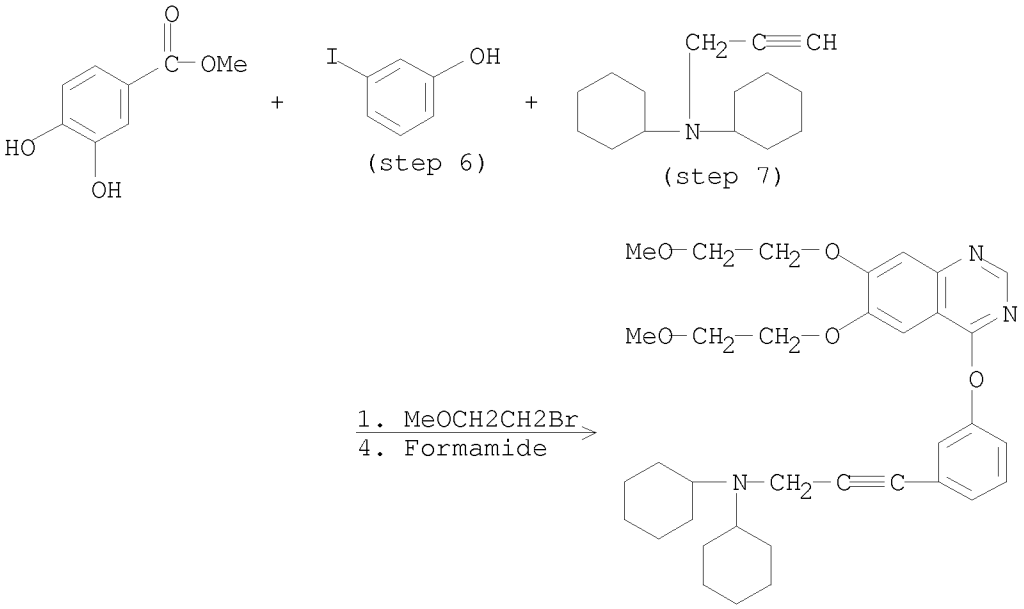
RX(143) OF 171 - 6 STEPS



60%

CON: STEP(3) 160 deg C
STEP(4) reflux
STEP(5) reflux
STEP(6) 60 deg C

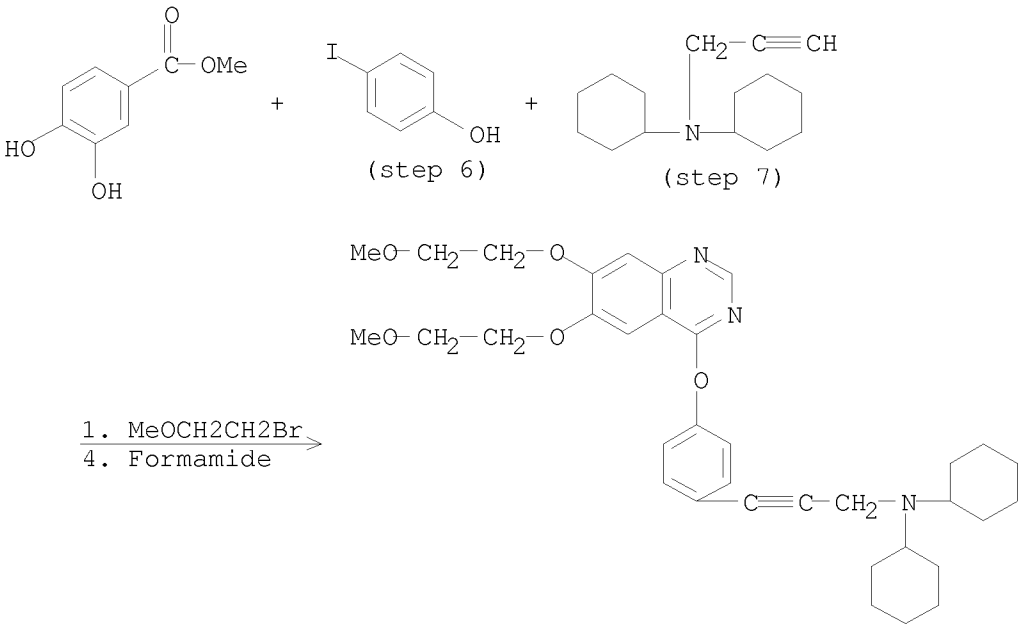
RX(146) OF 171 - 7 STEPS



24%

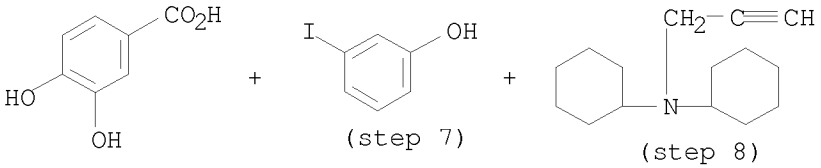
CON: STEP(1) reflux
STEP(4) 160 deg C
STEP(5) reflux
STEP(6) reflux
STEP(7) 60 deg C

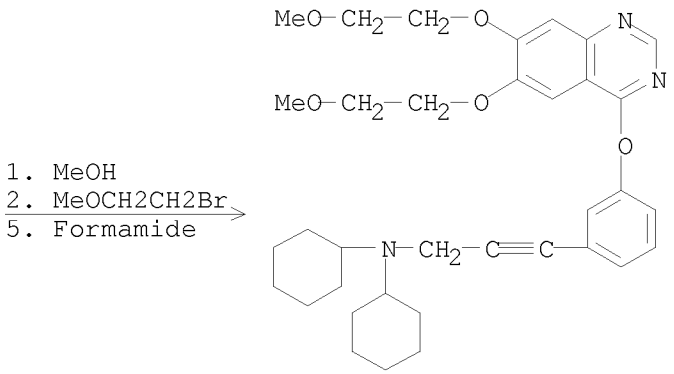
RX(147) OF 171 - 7 STEPS



CON: STEP(1) reflux
STEP(4) 160 deg C
STEP(5) reflux
STEP(6) reflux
STEP(7) 60 deg C

RX(150) OF 171 - 8 STEPS

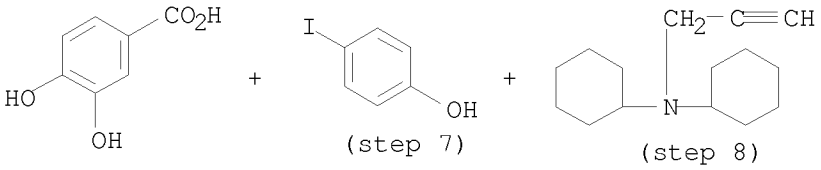




24%

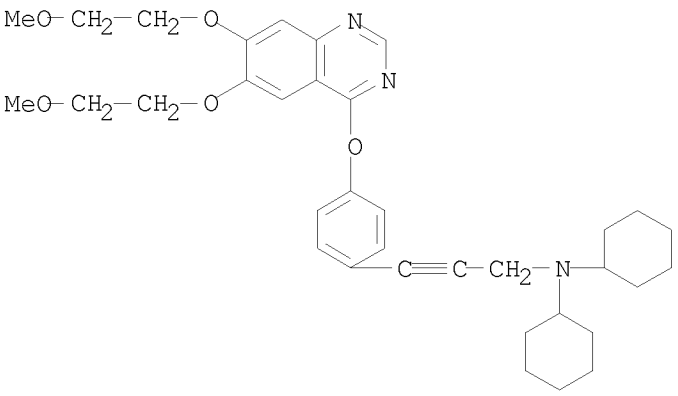
CON: STEP(1) reflux
STEP(2) reflux
STEP(5) 160 deg C
STEP(6) reflux
STEP(7) reflux
STEP(8) 60 deg C

RX(151) OF 171 - 8 STEPS



(step 7)

(step 8)

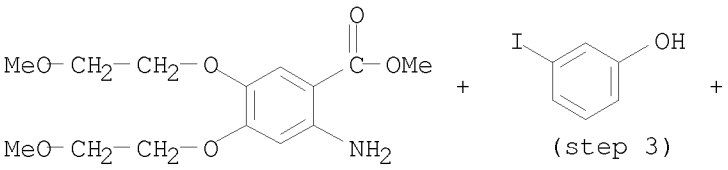


1. MeOH
2. MeOCH2CH2Br
5. Formamide

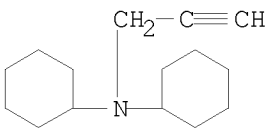
60%

CON: STEP(1) reflux
STEP(2) reflux
STEP(5) 160 deg C
STEP(6) reflux
STEP(7) reflux
STEP(8) 60 deg C

RX(154) OF 171 - 5 STEPS



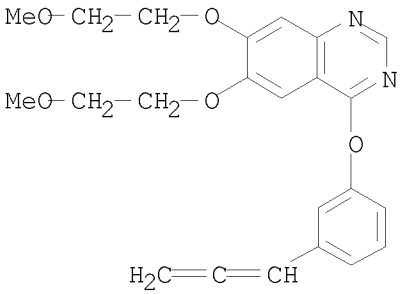
(step 3)



(step 4)

1. Formamide
2. EtN(Pr-i)2, POCl3, PhMe
3. K2CO3, Me2CHOH
4. Pd(PPh3)4, CuI, Et3N, MeCN
5. Pd complex, R:76858-94-1, CHCl3

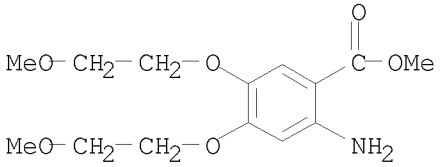
RX(154) OF 171 - 5 STEPS



55%

CON: STEP(1) 160 deg C
STEP(2) reflux
STEP(3) reflux
STEP(4) 60 deg C
STEP(5) 100 deg C

RX(155) OF 171 - 5 STEPS



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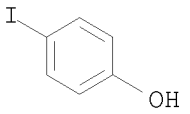
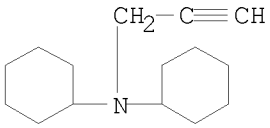


(step 3)

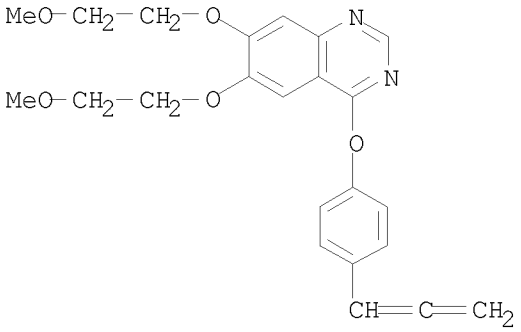
+



(step 4)

1. Formamide
2. EtN(Pr-i)2, POCl3, PhMe
3. K2CO3, Me2CHOH
4. Pd(PPh3)4, CuI, Et3N, MeCN
5. Pd complex, R:76858-94-1, CHCl3

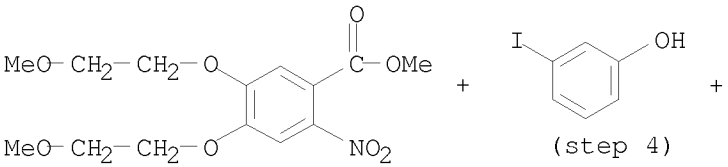
RX(155) OF 171 - 5 STEPS



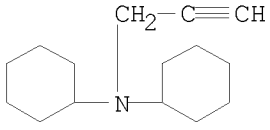
61%

CON: STEP(1) 160 deg C
STEP(2) reflux
STEP(3) reflux
STEP(4) 60 deg C
STEP(5) 100 deg C

RX(158) OF 171 - 6 STEPS

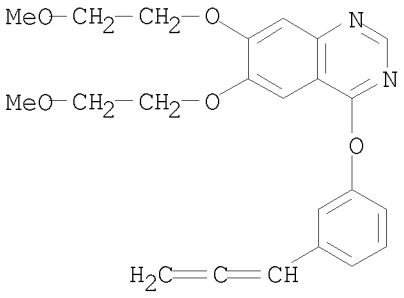


(step 4)



(step 5)

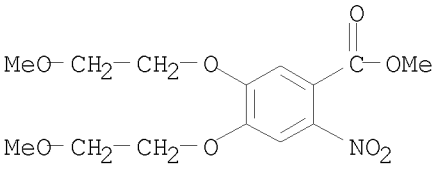
2. Formamide



55%

CON: STEP(2) 160 deg C
STEP(3) reflux
STEP(4) reflux
STEP(5) 60 deg C
STEP(6) 100 deg C

RX(159) OF 171 - 6 STEPS



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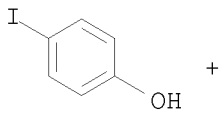
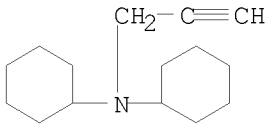


(step 4)

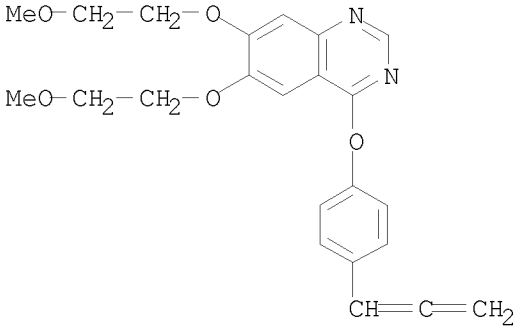
+



(step 5)

2. Formamide →

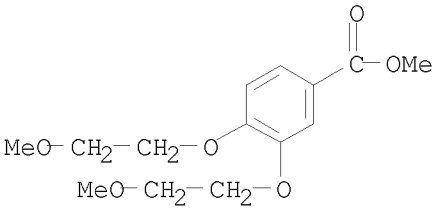
RX(159) OF 171 - 6 STEPS



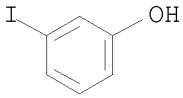
61%

CON: STEP(2) 160 deg C
STEP(3) reflux
STEP(4) reflux
STEP(5) 60 deg C
STEP(6) 100 deg C

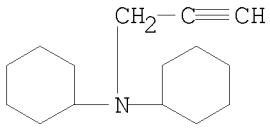
RX(162) OF 171 - 7 STEPS



+

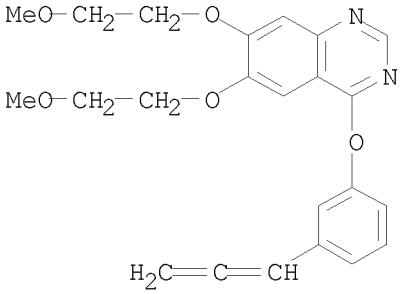


(step 5) +



(step 6)

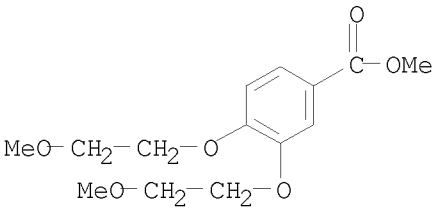
3. Formamide



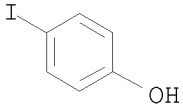
55%

CON: STEP(3) 160 deg C
STEP(4) reflux
STEP(5) reflux
STEP(6) 60 deg C
STEP(7) 100 deg C

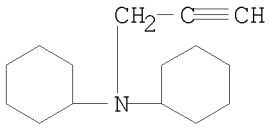
RX(163) OF 171 - 7 STEPS



+



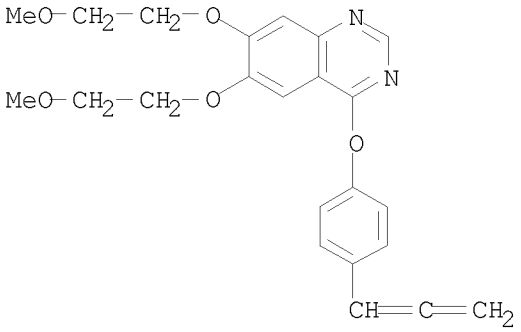
(step 5) +



(step 6)

3. Formamide

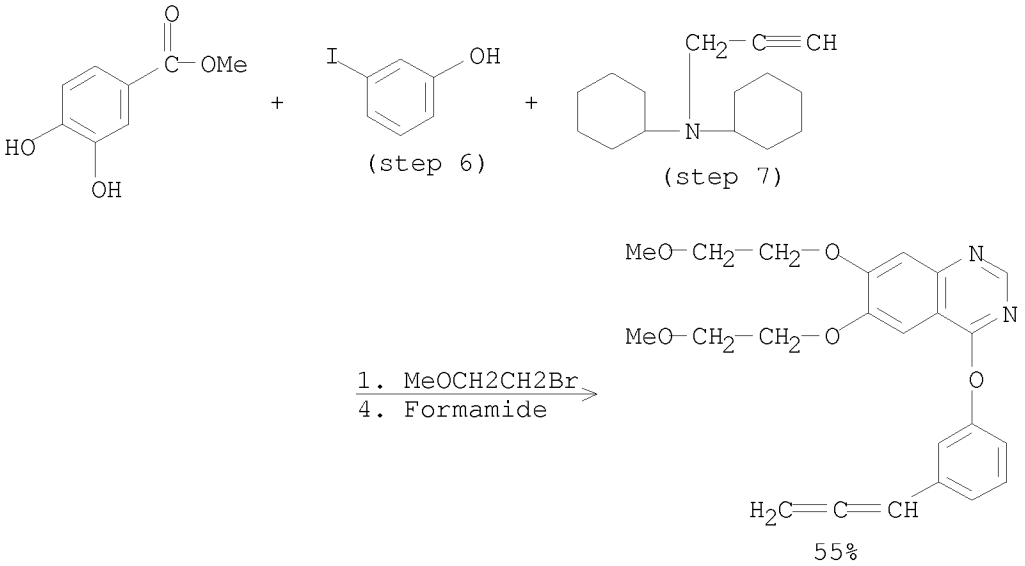
RX(163) OF 171 - 7 STEPS



61%

CON: STEP(3) 160 deg C
STEP(4) reflux
STEP(5) reflux
STEP(6) 60 deg C
STEP(7) 100 deg C

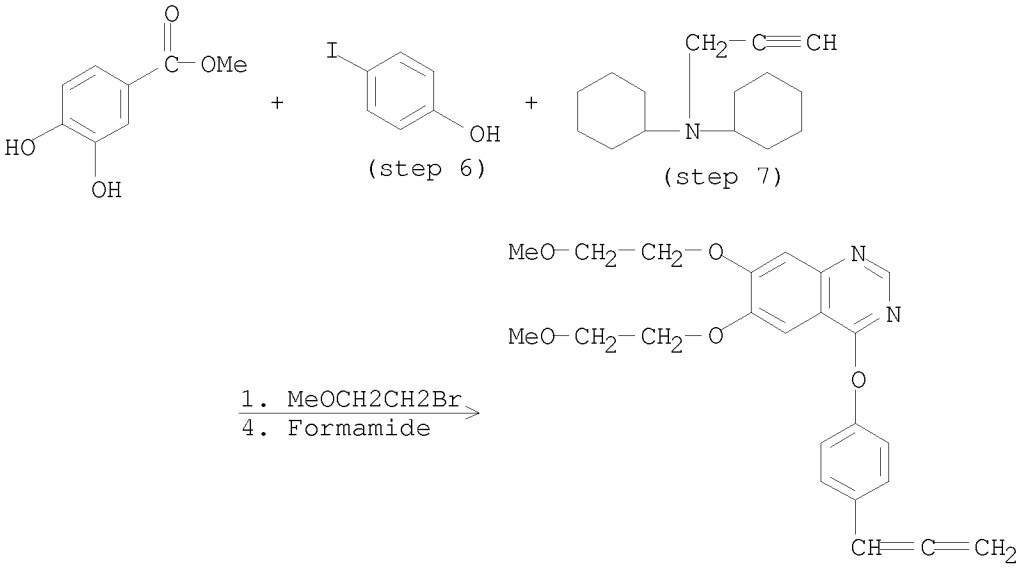
RX(166) OF 171 - 8 STEPS



55%

CON: STEP(1) reflux
STEP(4) 160 deg C
STEP(5) reflux
STEP(6) reflux
STEP(7) 60 deg C
STEP(8) 100 deg C

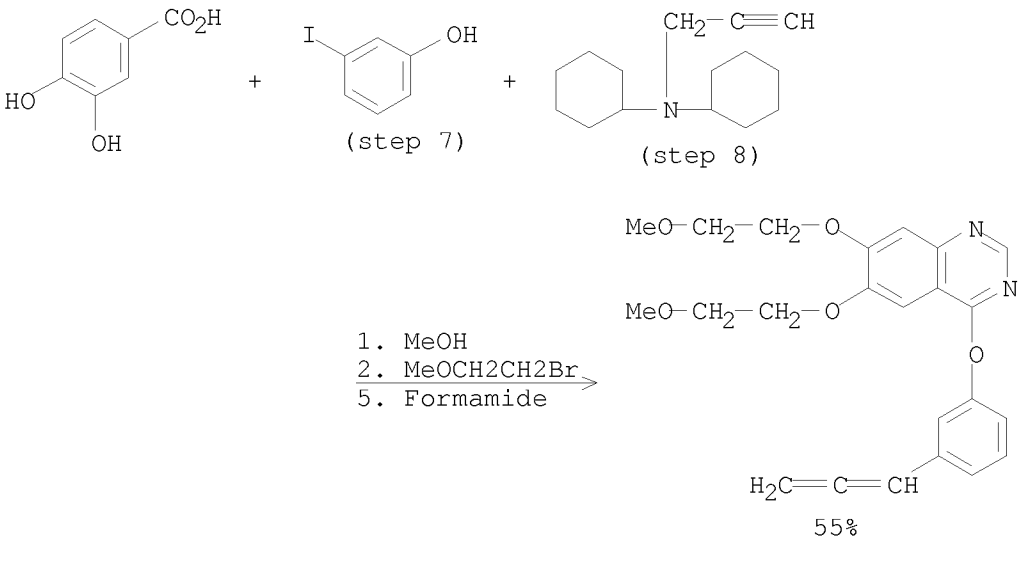
RX(167) OF 171 - 8 STEPS



61%

CON: STEP(1) reflux
STEP(4) 160 deg C
STEP(5) reflux
STEP(6) reflux
STEP(7) 60 deg C
STEP(8) 100 deg C

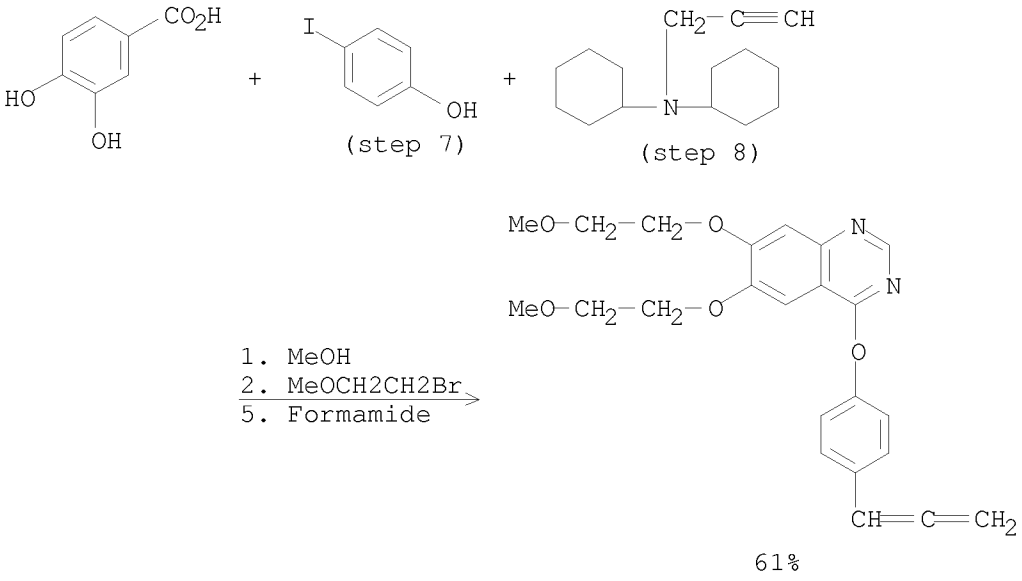
RX(170) OF 171 - 9 STEPS



55%

CON: STEP(1) reflux
STEP(2) reflux
STEP(5) 160 deg C
STEP(6) reflux
STEP(7) reflux
STEP(8) 60 deg C
STEP(9) 100 deg C

RX(171) OF 171 - 9 STEPS



61%

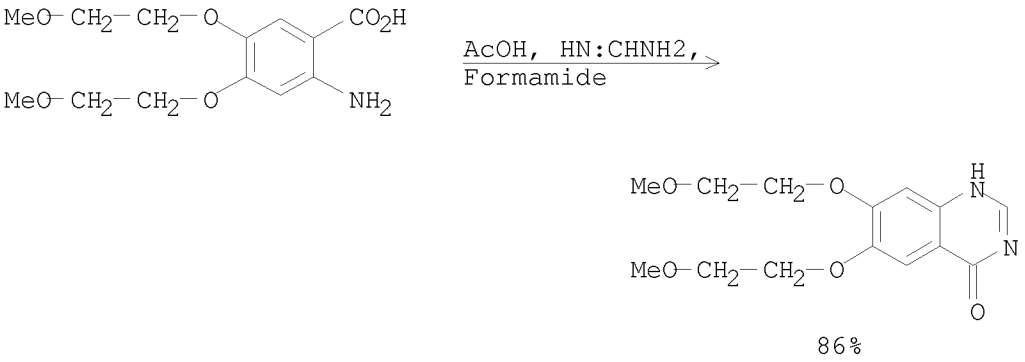
CON: STEP(1) reflux
STEP(2) reflux
STEP(5) 160 deg C
STEP(6) reflux
STEP(7) reflux
STEP(8) 60 deg C
STEP(9) 100 deg C

L3 ANSWER 6 OF 10 CASREACT COPYRIGHT 2008 ACS on STN
142:240390 Improved, high yield synthesis of 3H-quinazolin-4-ones, the key intermediates of recently developed drugs. Oerfi, Laszlo; Waczek, Frigyes; Pato, Janos; Varga, Istvan; Hegymegi-Barakonyi, Balint; Houghten, Richard A.; Keri, Gyoergy (Department of Pharmaceutical Chemistry, Semmelweis University, Budapest, Hung.). Current Medicinal Chemistry, 11(19), 2549-2553 (English) 2004. CODEN: CMCHE7. ISSN: 0929-8673. Publisher: Bentham Science Publishers Ltd..

AB Purine bases and their bioisosteric analogs are widely used as building blocks in combinatorial chemical Recently a great number of fused pyrimidine derivs. became known as potential drug mols. against various types of proliferative diseases, caused by over-expression of protein kinases. One of the most important compound families are quinazolines: e.g. the best inhibitor of EGFR tyrosine kinase is PD153035 (6,7-dimethoxy-4-(3'-bromophenyl)amino-quinazoline) [2] and IRESSA (gefitinib, ZD1839) [3], developed from this compound family, is presently the only one approved and

granted drug by the FDA for the treatment of advanced non-small-cell lung cancer (NSCLC). KF31327 (3-ethyl-8-[2-(4-hydroxymethylpiperidino)benzylamino]-2,3-dihydro-1H- imidazo[4,5-g]-quinazoline-2-thione dihydrochloride) from this group, showed significantly higher inhibitory activity on cyclic GMP-specific phosphodiesterase compared with those of sildenafil (Viagra). The synthetic procedures of the example compds. are based on imidoyl chloride intermediates that were prepared from the appropriate 3H-quinazoline-4-ones. Although the key intermediates, quinazoline-4-ones, have been known since more than hundred years, their synthetic procedures have been improved much only in the past ten years. In this paper we reviewed the efficient synthetic methods of quinazolin-4-ones; and presented a novel, reliable method for their synthesis. There was no considerable effect of microwave-, or traditional thermal activation on the yield and compound purity.

RX(27) OF 30



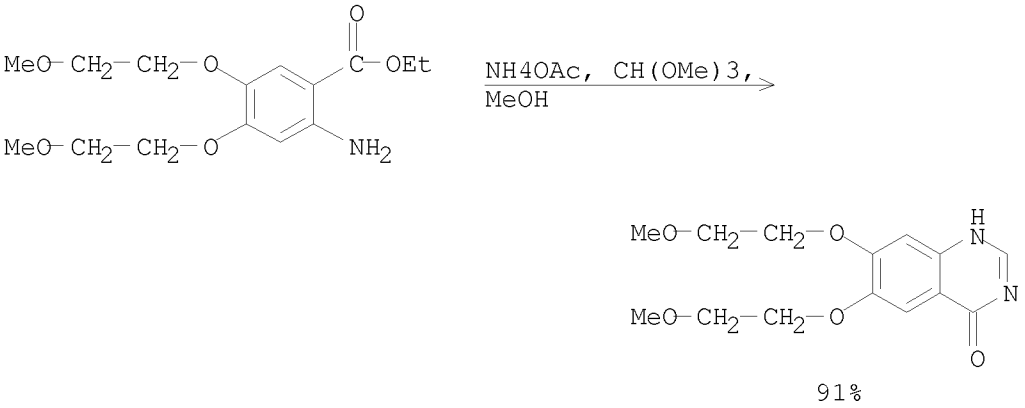
86%

NOTE: workup: hot aq. NaOH /charcoal decolorization and acidification (purity 87%)
CON: 2 hours, 160 deg C

L3 ANSWER 7 OF 10 CASREACT COPYRIGHT 2008 ACS on STN
142:219298 Process for preparation of 6,7-bis(2-methoxyethoxy)quinazolin-4-one. Nishino, Shigeyoshi; Hirotsu, Kenji; Shima, Hidetaka; Oda, Hiroyuki; Suzuki, Shinobu (Ube Industries, Ltd., Japan). PCT Int. Appl. WO 2005012264 A1 20050210, 18 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (Japanese). CODEN: PIXXD2. APPLICATION: WO 2004-JP10965 20040730. PRIORITY: JP 2003-282696 20030730.

AB This invention pertains to a method for producing 6,7-bis(2-methoxyethoxy)quinazolin-4-one, which comprises reacting Et 2-amino-4,5-bis(2-methoxyethoxy)benzoate with a formic acid compound in the presence of an ammonium carboxylate. For example, Et 2-amino-4,5-bis(2-methoxyethoxy)benzoate (preparation given) was reacted with Me orthoformate in MeOH in the presence of NH4OAc to give the title compound (91%). This invention provides a convenient method to prepare the title compound from Et 2-amino-4,5-bis(2-methoxyethoxy)benzoate in high yield.

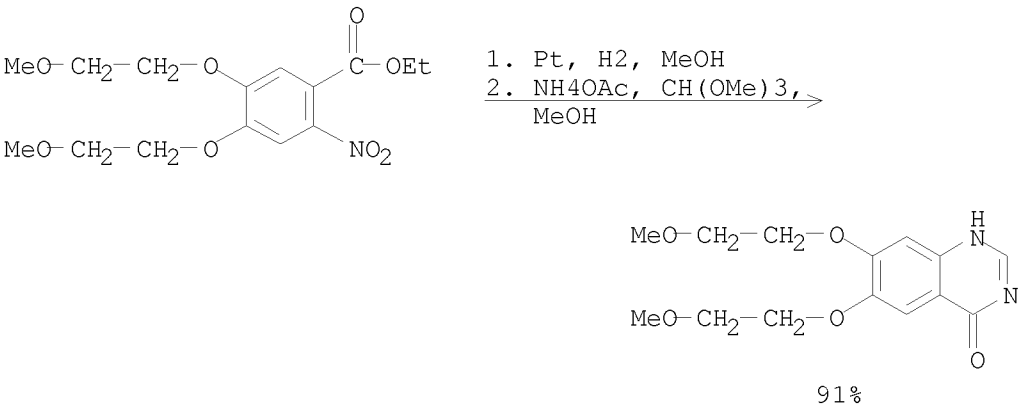
RX(4) OF 10



91%

CON: 7 hours, 60 - 70 deg C

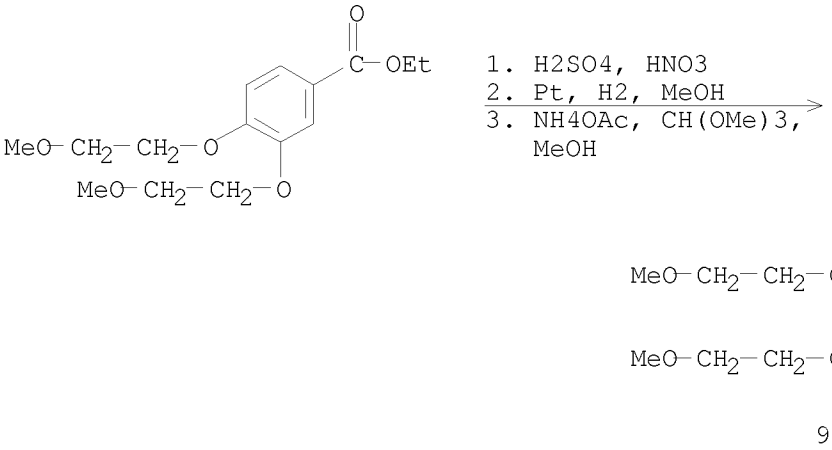
RX(7) OF 10 - 2 STEPS



91%

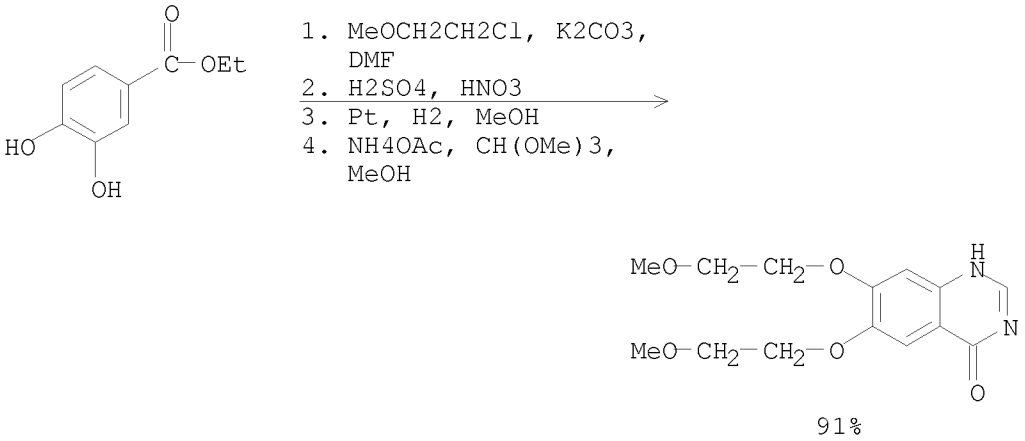
CON: STEP(1) 6 hours, 50 - 60 deg C
STEP(2) 7 hours, 60 - 70 deg C

RX(9) OF 10 - 3 STEPS



CON: STEP(1.1) room temperature -> 70 deg C; 2 hours, 70 deg C
STEP(2) 6 hours, 50 - 60 deg C
STEP(3) 7 hours, 60 - 70 deg C

RX(10) OF 10 - 4 STEPS

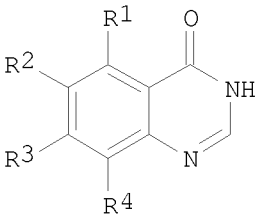


CON: STEP(1) 9 hours, 90 - 100 deg C
STEP(2.1) room temperature -> 70 deg C; 2 hours, 70 deg C
STEP(3) 6 hours, 50 - 60 deg C
STEP(4) 7 hours, 60 - 70 deg C

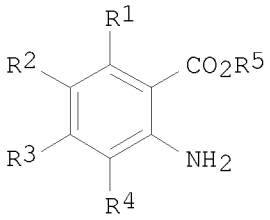
L3 ANSWER 8 OF 10 CASREACT COPYRIGHT 2008 ACS on STN
139:164805 Process for producing 3,4-dihydroquinazolin-4-one derivatives. Nishino, Shigeyoshi; Hirotsu, Kenji; Shima, Hidetaka; Harada, Takashi; Oda, Hiroyuki; Takahashi, Takeshi; Suzuki, Shinobu (Ube Industries, Ltd., Japan). PCT Int. Appl. WO 2003064399 A1 20030807, 101 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR.

(Japanese). CODEN: PIXXD2. APPLICATION: WO 2003-JP805 20030128. PRIORITY: JP 2002-17957 20020128; JP 2002-40929 20020219; JP 2002-82607 20020325; JP 2002-168443 20020610; JP 2002-178661 20020619; JP 2002-246657 20020827; JP 2002-326752 20021111; JP 2002-349456 20021201.

GI



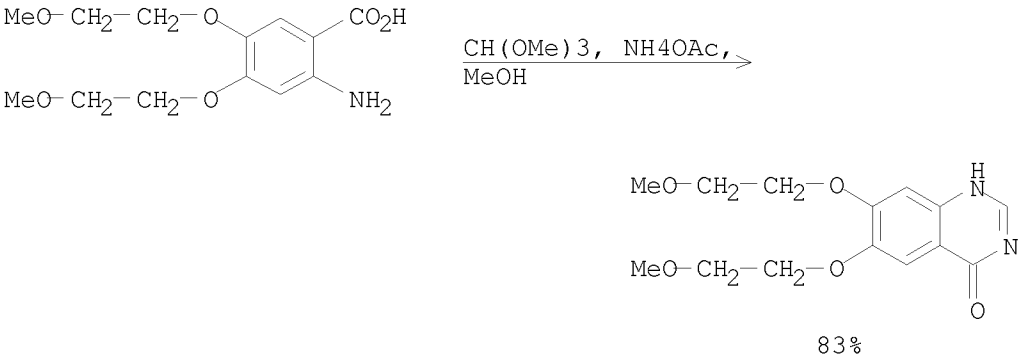
I



II

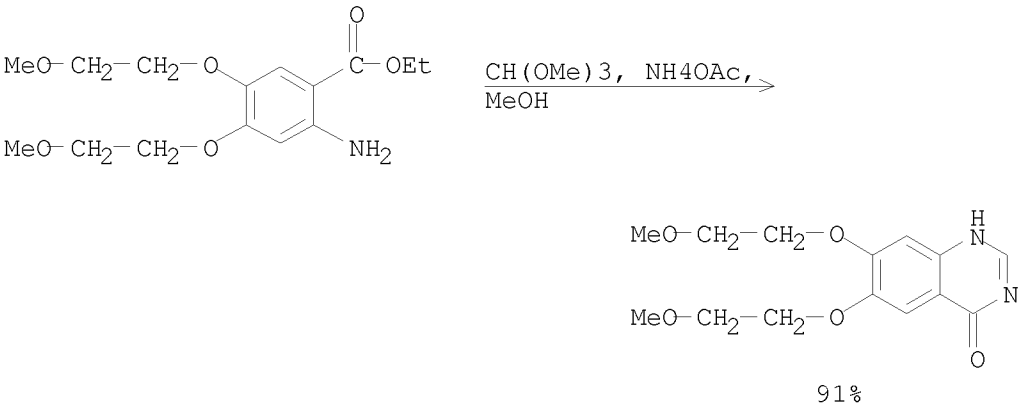
AB Disclosed is a process for producing a quinazolin-4-one derivative represented by the following formula (I) (wherein R1, R2, R3, and R4 each represents a group not participating in the reaction and R1, R2, R3, and R4 may be bonded to each other to form a ring) which comprises reacting an anthranilic acid derivative represented by the following formula (II) (wherein R1-R4 are defined as above; R5 represents hydrogen or a hydrocarbon group) with a formic acid derivative (in particular orthoformate ester) in the presence of an ammonium carboxylate. This process gives 3,4-dihydroquinazolin-4-one derivs. I, which are useful as intermediates for drugs and agrochems., from anthranilic acid derivs. in high yields in a simple method under mild conditions and is industrially suitable. Thus, 5-methoxy-4-(3-chloropropoxy)anthranilic acid Me ester 161.5, Me orthoformate 156.5, ammonium acetate 113.7 g, and 300 mL MeOH were added to a 1,000 mL stainless steel pressure vessel, allowed to react at 90-95° and 0.1-0.3 MPa for 8 h, treated with 600 mL H2O, stirred at 0-10° for 1 h, and filtered to give, after washing the crystals with 600 mL H2O and drying them at 60° under reduced pressure, 94% 6-methoxy-7-(3-chloropropoxy)quinazolin-4-one (152.8 g).

RX(11) OF 112



NOTE: high pressure cyclocondensation in a stainless pressure vessel
CON: 8 hours, 95 deg C

RX(12) OF 112

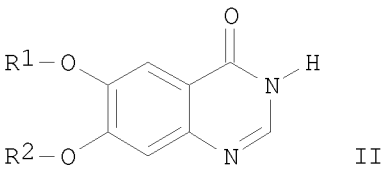


91%

NOTE: high pressure cyclocondensation in a stainless pressure vessel
CON: 6 hours, 110 deg C

L3 ANSWER 9 OF 10 CASREACT COPYRIGHT 2008 ACS on STN
139:164804 Preparation of quinazolinone derivatives and 4,5-substituted-2-formylaminobenzamides as intermediates for said quinazolinones. Shirai, Masashi; Furuya, Toshio (Ube Industries, Ltd., Japan). PCT Int. Appl. WO 2003064377 A1 20030807, 30 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (Japanese). CODEN: PIXXD2. APPLICATION: WO 2003-JP562 20030122. PRIORITY: JP 2002-19583 20020129; JP 2002-77880 20020320.

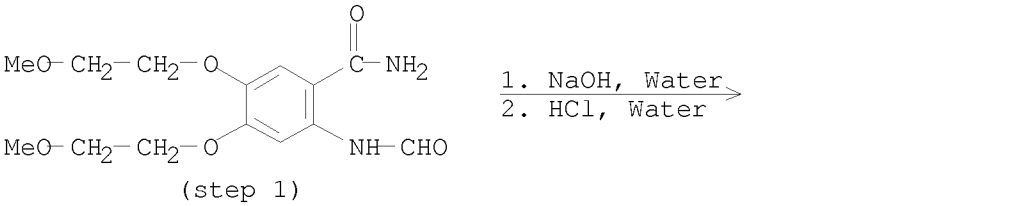
GI



II

AB 4,5-Substituted-2-formylaminobenzamides (I) are produced by reacting the corresponding aminobenzamides with formic acid in an organic solvent, and I are further converted into 6,7-substituted-quinazolin-4-ones of the general formula II [R1, R2 = H, (un)substituted alkyl, etc.] by cyclization in the presence of a base. I are pharmaceutical intermediates. 6,7-Dimethoxy-3H-quinazolin-4-one was prepared in 93% yield by the above-mentioned process.

RX(7) OF 12

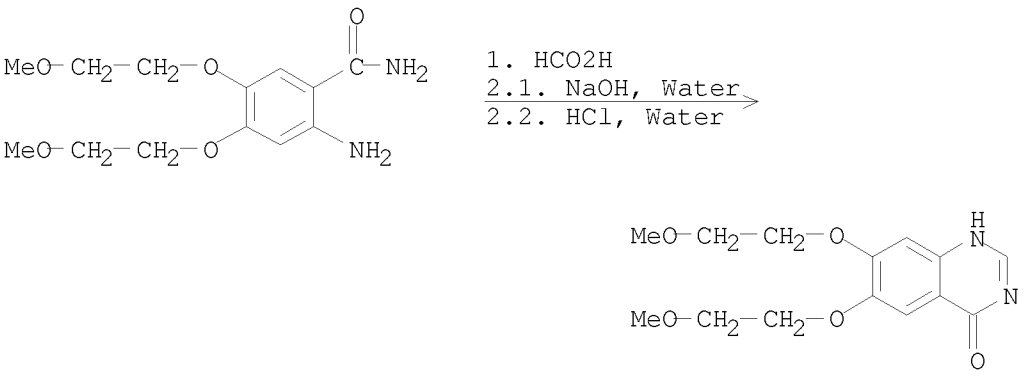


(step 1)

84%

CON: STAGE(1) 30 minutes, 25 deg C, pH 13.5
STAGE(2) pH 7.6

RX(11) OF 12 - 2 STEPS



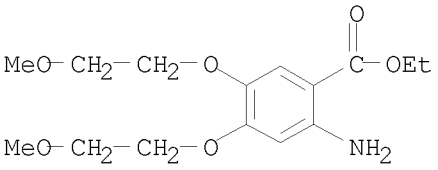
84%

CON: STEP(1.1) room temperature -> 5 deg C; 5 deg C -> 25 deg C;
48 hours, 25 deg C
STEP(2.1) 30 minutes, 25 deg C, pH 13.5
STEP(2.2) pH 7.6

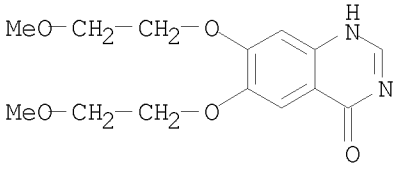
L3 ANSWER 10 OF 10 CASREACT COPYRIGHT 2008 ACS on STN
137:263058 Preparation of quinazoline derivative as intermediates for antitumor agent. Wang, Wi-Chi; Iseki, Eiichi; Imamiya, Katsuyuki (Sumika Fine Chemicals Co., Ltd., Japan). Jpn. Kokai Tokkyo Koho JP 2002293773 A 20021009, 9 pp. (Japanese). CODEN: JKXXAF. APPLICATION: JP 2001-100183 20010330.

AB 6,7-Bis(2-methoxyethoxy)-4(1H)-quinazolinone, an intermediate for the antitumor agent N-(3-ethylphenyl)-6,7-bis(2-methoxyethoxy)-4-quinazolinamine, is prepared in several steps from Et 3,4-dihydroxybenzoate and 2-methoxyethyl mesylate via cyclocondensation of Et 2-amino-4,5-bis(2-methoxyethoxy)benzoate with ammonium formate.

RX(5) OF 15

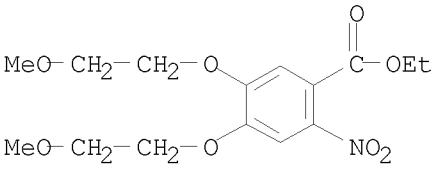


Ammonium formate,
Formamide

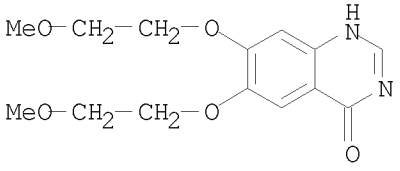


80%

RX(9) OF 15 - 2 STEPS

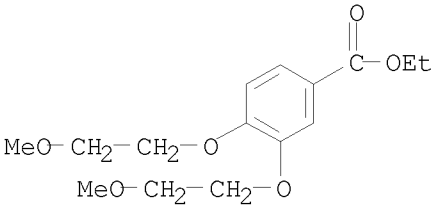


1. Pt, H2, MeOH
2. Ammonium formate,
Formamide

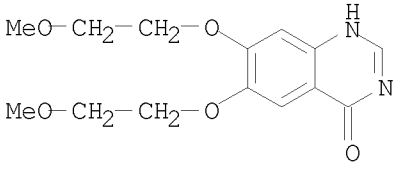


80%

RX(13) OF 15 - 3 STEPS

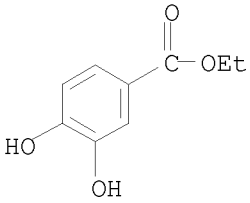


1. H2SO4, HNO3, AcOH
2. Pt, H2, MeOH
3. Ammonium formate,
Formamide



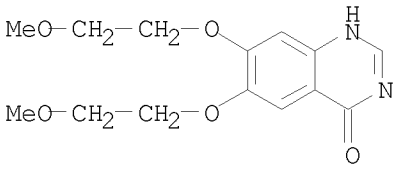
80%

RX(14) OF 15 - 4 STEPS



+ MeO–CH2–CH2–O–S(=O)(=O)–Me

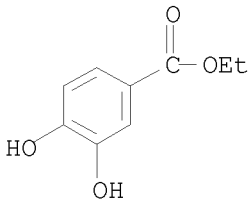
1. Bu4N.I, K2CO3, Me2CO
2. H2SO4, HNO3, AcOH
3. Pt, H2, MeOH
4. Ammonium formate, Formamide



80%

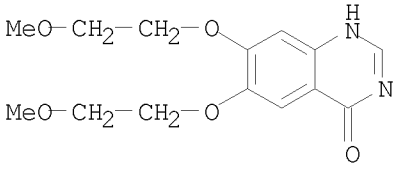
RX(15) OF 15 - 5 STEPS

Cl–S(=O)(=O)–CH3 +



(step 2)

1. MeCH2CH2OH, N-Methylmorpholine, THF
2. Bu4N.I, K2CO3, Me2CO
3. H2SO4, HNO3, AcOH
4. Pt, H2, MeOH
5. Ammonium formate, Formamide



80%

=>